

THE PRACTITIONER

No 9257

JULY, 1945

Volume 155

ORGANIZATION OF A CANCER SERVICE

By SIR E ROCK CARLING, M.B., F.R.C.P., F.R.C.S.

Consulting Surgeon, Westminster Hospital, Consultant Adviser in Surgery, Emergency Medical Service, Consultant Adviser on Casualty Services, Ministry of Home Security, and Ministry of Health

WHY a "cancer service"? Why not a "medical service"? Because whilst there is an Act on the statute book relating to cancer and suspected cancer, there is none as yet for the provision of a universal medical service. Doubtless the Cancer Act will be submerged in forthcoming legislation but, since payment of grant follows ministerial approval of a scheme, progress has been made which anticipates, and cannot fail to affect, the pattern of a complete service.

PRESENT POSITION

Existing assets—There are already available large numbers of surgeons, some, but not enough, radiotherapists, with an increasing number of biophysicists, many biochemists and other pathologists. There are physicians indispensable in diagnosis, others who care for patients in the irremediable stages of the disease, and still others interested in therapeutic trials which might be called "humoral." There are considerable numbers of hospital beds for patients.

Defects—Yet, at a time when many patients are cured of cancer or survive for long years without sign of disease, others die of cancer without ever being treated, and many more first present for treatment when too bad for hope of "cure." What is the matter with the present arrangements? First, there are not enough contacts close at hand for preliminary investigations, secondly, diagnosis is attempted without all the resources to make it sure, and, thirdly, the operative work is not always carried out under conditions calculated to provide the best of which surgeons are capable. For one thing, they work too often in cottage hospitals and nursing homes where there is no resident. Moreover, it cannot be denied that much surgery is done by those who, whatever their technical skill, cannot obtain a wide enough experience to make them fully competent; nor that much radiotherapy has been done by men whose first interest is radio-diagnosis, and who have not the physicist help which the most experienced radiotherapists find essential.

There seems to be general agreement that there ought to be greater provision of hospital beds in the country. That deficiency cannot be made good for a long time to come. What could be done is to pool all existing beds and utilize them to the greatest advantage. Public hospitals accept patients from within their rateable areas. If they take them by user agreement from beyond their own frontiers, the arrangements may work, or the machinery may have so much dust in the cogs that it does not operate effectively. Voluntary hospitals accept patients from their natural catchment areas, but rarely have enough beds for their commitments and are apt to dispute the geographical limits of their legitimate field with near neighbours.

who need their share of voluntary gifts and "contributory" resources. Generally speaking the one type of hospital has a small whole-time staff, much of it not highly experienced, the other a much larger part-time staff, of which the seniors at least are long-experienced men.

COMBINED OPERATIONS

In almost any large county borough it would be possible, by combining resources of all kinds—beds, staff, technical assistants, nurses, pathologists, out-patient departments, special units, clinics—to provide preliminary investigation centres, diagnostic centres and treatment of a high order for 90-95 per cent. of cases, and the area to be covered by this local organization can be defined by road and rail transport convergence, by the habits of the commercial and marketing world. Big towns grow up where they are wanted. So does a metropolis. Where banking, insurance, exchange, wholesale trading, the law, the church and the administration have their focus, there is a provincial university with the same sphere of influence. There, naturally, must be the headquarters of medicine, for thither go the ablest, the most adventurous, the most confident of younger citizens, to make good. All this, with contingent economic necessity, has led naturally to undue concentration of talent at the centre. Big cities have no monopoly of skill and competence, but, for the purposes of a cancer or of any other medical service, greater dispersal must be accomplished. Fortunately, distances which were too great for horse-drawn transport are trivial to the motor car and will be even less to the ubiquitous aeroplane of the future. So university duties can now be carried out by those domiciled fifty or a hundred miles away.

The family practitioner—There can be no doubt that the best first contact for the patient with any organization is a good family practitioner in whom he has complete confidence. Even for the family practitioner it is important that there should be an undisturbed session, where with nurse and clerk or secretary he can, at regular intervals, see all those patients of his, including those with suspected cancer, who may need a quiet half-hour's consideration. The fact must be admitted that the "doctor-patient relation" is in too many cases not good enough to ensure against many cases slipping through the net. So "family" hospital, or clinic, or "health-centre" facilities should be available. The practitioner's path, as well as the patient's, must be made easy. Contact of a suspect with the outlying tentacles of the organization ought to ensure a straight course just as far along the chain of posts towards the centre, where the exceptional case finally should arrive, as may be necessary.

The intermediate post or stage should be the "district hospital" and the district hospital should embrace all the resources congregated in its immediate locality.

Court of appeal—Finally, there should be the group of hospitals serving the need of the faculty of medicine of a university. Here, although there may be brilliant exceptions, is sure to be found the cream of medical skill, here will be those special clinics and divisions for diagnosis and treatment that demand and serve a large population, a population as large as that of four, six, eight or even ten district hospitals.

There should, then, be three main grades of hospitals, within these grades, as occasion and special circumstances dictate, there may be associated or sub-

or even duplicate, orders. Of the three main types, the "family" hospital, the "district" hospital and the "central" teaching hospital, it should be clear that although the first is the outlying contact point, the second will contain within it a local contact point, its out-patient department; and the third, whilst functioning as a court of appeal for the exceptional case and for training, will also act as one of its own district hospitals, and through that as a local contact point.

Sharing special clinics —As regards medium-sized district hospitals, it may be that grouping will be the readiest means of providing adequate units for those specialisms which can serve a population larger than that for which a single district hospital usually caters. Whilst every family hospital will be a preliminary investigation centre for cancer, as for other disorders, every district hospital, properly constituted, will be a *diagnostic* centre, but not necessarily a treatment centre for every form of cancer. Thus, if three district hospitals make a group, one may have a major urological unit, one a major gynæcological unit, another, for example, a thoracic unit. It will be logical to send the cases of malignant disease of those systems to the care of the specialists in charge of those units, and not to retain them all in one hospital. If X has his main clinic in hospital A, in B and C he will have juniors and deputies. Z, with his own clinic in B, in C and A will have juniors, and so on, and in this relation there will be a common staff. Its object should be to make the "district" hospital or group the mainstay of the whole system, doing practically the whole work of its area. The "teaching" hospital may well be a group of institutions, and in a big city there may be a number of district hospitals.

HEADQUARTERS

It may well happen at the headquarters that, for example, a neurological unit, serving the whole area, is not in the undergraduate hospital but in one of the district hospitals nearby—whether voluntary or local authority—and there tumours of the brain and cord should go for treatment. As another example, radiotherapy ought to be centralized, but, if special geographical or other conditions dictate one or more associated centres, the staff must be one. There must be no attaching a junior therapist to a unit where the number of cases is insufficient to give full experience, and keeping him there in isolation.

Seconding —The experience of the man temporarily seconded to the lesser unit ought to be that provided by the greater, to which he should return from time to time, and of which he must always feel himself a part. It must be open to the head of the central unit to require the removal to the centre, of any case for which he feels that efficient treatment cannot be given peripherally. For example, if there be beam therapy available at the centre and that method is the one of choice for a particular condition, to it the patient should go. When circumstances have dictated subdivision of the work, the less well-equipped institution which has been allowed to retain radiotherapy because of *amour propre*, vested interest, or even the one really defensible reason, distance, should not be allowed to retain a patient whose interests require his access to the greatest facilities and skill.

CONCENTRATION

In the field of radiotherapy the experience of the Radium Commission which extends over fifteen years, proves that single centres can cater for the needs of

three million people, perhaps more, and that only where geographical condition prohibit provision on a larger scale should a headquarters centre exist for as small a number as a million. With less, the staff will have insufficient experience of the rarer tumours and, with the increasing complexity, cost and potency of modern apparatus, it will be impossible to provide full facilities, save in a few places. Apart from initial cost, the running costs of the expert staff required to control the apparatus would be substantially as great for the smaller as for the larger units.

REGIONAL SERVICES

Experience of regionalized services, of which a great deal is now available, goes to show that centring upon universities is a most valuable means of securing a high standard of work throughout their sphere of influence. As regards hospitals that undertake any teaching duties, undergraduate or postgraduate, the universities will, in future, have financial sanctions behind their academic influence.

Those who set out to decide the pattern of any organization will be sure to use all the assets available. Organization is needed to eliminate waste of effort and failure to "deliver the goods." Where neither waste nor failure exist there is no need for change. Is there any large district in the country of which no criticism is valid?

THE PATIENT'S POINT OF VIEW

An organization for the treatment of cancer should be looked at from the patient's point of view. If the faintest anxiety arises in his mind, or in the minds of those about him on his behalf, contact with the whole system should be as easy as with the postal system, the practitioner's red lamp should be as familiar as the pillar-box, the family hospital as easy of access as the village post office, the path to the G.P.O. no more certain than that through the chain of institutions to the hospital headquarters. The G.P.O. cannot function unless the citizen uses the pillar box, for it is the foundation of the system. So must be the family practitioner. Postal packets go no farther along the road than they need, and in any district the central post office does the bulk of the local work. So must the district hospital. But if the services of the G.P.O. be needed they function without fail. So it must be with the court of appeal for the exceptionally difficult case. The course to headquarters must be automatic and unquestioned. *Via* the G.P.O. any desired place in the Empire can be reached. If something is to be found in Toronto that Great Britain cannot offer, it should be reachable or its peculiar benefit be brought to patients here. Like the postal system, the traffic must be two-way. If the patient, like the parcel, has a straight road to the centre, the track is equally open for the distribution of specialist skill from the district to the family hospital or the home, from headquarters to the district hospital and, if need be, beyond it to the family hospital and the consulting room. Some such organization will transform the existing resources into a more efficient and more homogeneous service. When it is established for cancer it will be available for all ill-health. In any event, cancer cannot be abstracted from other illness and diagnosed or treated in isolation.

A great uncertainty overhangs the administrative structure of the future health service, but there is no uncertainty as to the capacity of the profession itself, *now*, to organize its services of every kind, merely by rearrangement of duties, in such a way that the patient with cancer obtains the best that is available. And if for cancer, then for all his ills.

RECENT ADVANCES IN KNOWLEDGE OF MALIGNANT DISEASE

By W E GYE, MD, FRCP, FR.S

*Director of the Imperial Cancer Research Fund, Professor of Experimental Pathology,
Royal College of Surgeons, London*

CANCER research touches many sciences—chemistry, physics, genetics, bacteriology and biology, as well as pathology—and there have been advances in all these fields. Any account of recent advances is necessarily biased by special experience, the chemist would naturally relate the progress made in preparing pure chemical compounds which induce cancer in animals and would describe at length the theories which have been advanced to explain their action, the physicist would weight his story in favour of the action of X-rays, whilst the geneticist and biologist would discuss genes and mutations. It is generally found that the historical approach clarifies any discussion of an important problem in science, and it is especially so in cancer because the discoveries of the pathologists of the nineteenth century and the early work of experimental pathologists—Jensen, Bashford, Ehrlich, Loeb and many others—are often ignored or forgotten in the present spate of publications. Yet it is of the utmost importance to realize that the fundamental nature of the disease process called cancer or “malignant disease” was discovered long ago, that the problems to be solved were clearly realized and stated, and that much of the preliminary work was done. The work of the pioneers of cancer research is not now sufficiently understood or appreciated, and it is a consequence of the neglect of their writings that any wild speculation concerning cancer causation receives attention. It is therefore right to preface a review of recent advances in the knowledge of malignant disease with a restatement of the nature of cancer and of the problems awaiting solution. It is only thus that the significance of any “discovery” can be assessed.

THE PATHOLOGY OF CANCER

Cancer in its clinical manifestations is a disease of cells and not of the body as a whole. When mammary epithelium, for example, assumes the malignant state the cells begin to grow independently of body needs, and continue to grow, in spite of any growth restraints of the general organism. Metastases may occur in remote parts of the body—in lymph nodes, brain or in bones—and the metastases consisting of mammary epithelium grow independently of the original tumour and of any remote cause which may have caused the normal breast epithelium to assume the malignant state. This phenomenon is most clearly represented by experimental studies of mammary cancer in mice. It was discovered nearly fifty years ago that approximately 5 per cent of female mice develop cancer of the breast; the early cancers begin to appear in middle life, and as the mice become old more and more cancers appear. In other words, the age incidence for mice is the same as for

human beings. Fragments of living cancer cells, grafted under the skin of normal mice, grow and form what are called daughter tumours. The process can be repeated indefinitely, a fragment from a daughter tumour is transplanted to young normal mice and again it grows and forms another tumour, and so the process can be repeated apparently for ever. Certainly this process of keeping the malignant cells alive has been carried on, generation after generation, for more than forty years. The cancer cells are apparently endowed with immortality. Now it is of cardinal importance to realize that the daughter tumours are formed by proliferation of the implanted cells, there is no infection of host cells, and the conclusion may justly be drawn that the cells living in mice to-day are the lineal descendants of cancer cells which started, for reasons unknown, on their career of malignancy in a single mouse more than forty years ago.

From all this, and from pathological investigations on human cancer, it is certain that in cancer the stimulus to growth resides in the cancer cell itself. It may be stated with confidence —

- (1) That cancerous growth, once started, is not self-limited
- (2) That the cancer cell carries its own growth stimulus
- (3) That cancerous growth is not controlled by those forces within the body which limit physiological growth
- (4) That a cancer grows at the expense of the body
- (5) That cancerous growth is limited only by the life of the host.

In all these respects cancerous growth differs from physiological growth, the properties named are summed up by saying that the growth of cancers is autonomous. It is in this respect that cancer is unique, and it is not surprising that the majority of workers in cancer research look upon cancer as a single disease process, ultimately explicable as a consequence of a universal cause, in spite of the fact that malignant growths vary in structure, in clinical and biological qualities and may be artificially induced in a number of ways. This opinion, that there is, or may be, a universal cause for the unique phenomenon of autonomous growth, is the working hypothesis of cancer research and refers only to the intracellular or proximate causation of the disease, it is not related in any way to the numerous remote causes which it is known may operate before a tumour actually starts.

Causation of cancer is therefore divisible into two parts, first the causes, which are numerous, which operate on normal tissues precedent to the formation or evolution of true cancerous cells, and, second, the intracellular cause which operates within the cancer cell itself, and which drives the cell to divide and multiply beyond the needs and against the physiological integrity of the body. If these distinctions, which have been described and recognized by all the eminent workers in cancer research, are borne in mind, the significance or apparent lack of significance of any of the papers or memoirs on cancer in the now truly gigantic mass of literature which is poured from the presses of the world may readily be estimated. To the chemist, for example, it is usually sufficient to find a chemical compound which, applied to the skin, will start a squamous epithelioma, he is satisfied that the epithelioma has been caused by his compound, and, of course, in a rough sense he is right. But deeper inquiry leads to the desire to know what cause is operating within the cell, conferring the remarkable power of unlimited prolifera-

tion of a particular kind. For, it must be noted, the presence of the chemical compound is not necessary for the continuation of the tumour; once the tumour has been started it carries on as a malignant cell without any artificial aid. This is evident from the fact that metastases, remote from the site of application of the chemical substance, continue to grow after the primary tumour has been excised. It is even more evident in the epitheliomas which form on the basis of X-ray dermatitis. These may occur years after the patient has been exposed to the action of X-rays. It is still more convincingly demonstrated by the fact that tumours which have been induced by chemical substances, or by physical agents, such as X-rays, heat or ultra-violet light, or by the subtle action of gross parasites, are successfully transplanted in generation after generation of animals which have never been exposed to any one of these chemical or physical insults. In like manner, the geneticist is satisfied if, by careful breeding, strains of cancer-susceptible or cancer-resistant animals are evolved, the problem is then merely an exercise in genetics, and the interaction of genes becomes all important. To the pathologist these are merely individual aspects of the cancer problem, related almost invariably to the remote causes of cancer.

Therefore in this article, recent advances will be discussed under the two headings, remote, and intracellular or proximate causes of cancer.

REMOTE CAUSES OF CANCER

Chemical carcinogenic substances—In the uneasy period between the two wars with Germany, the single greatest advance in the subject of chemical causation of cancer was made by Kennaway, Cook, Hieger and their collaborators, working at the Royal Cancer Hospital. These workers prepared a series of pure chemical compounds, the first of which was 1,2,5,6-dibenzanthracene, which, when applied to the skin, caused the formation of epitheliomas, or injected subcutaneously, where connective tissues are acted on, caused sarcomas. In 1916, during the first European war, two Japanese workers, Yamagiwa and Itchikawa, had proved that long-continued application of coal tar to the skin of the rabbit elicited epitheliomas. That this occurs in men whose work in industry involves contact with coal tar has long been known. Even longer, since the eighteenth century in fact, it has been known that soot may start epitheliomas in man. The experimental induction of cancer in animals by these crude means was of importance because a method of studying the early stages of cancer formation was provided. But coal tar fell far short of the ideal method, because of the massive inflammatory reactions which are provoked long before the malignant processes become evident. Moreover, in the world of ideas, the action of coal tar appeared to be connected with the belief that chronic irritation is an essential preliminary to malignancy. Kennaway's contribution to the subject is all important in proving—first, that extensive general irritation of any kind is not necessary to the formation of tumours, second, that the irritation required need only be microscopic; third, that it is provided only by certain compounds and is dependent upon their chemical structure, and, fourth, that perfectly pure compounds possess the property now universally designated as carcinogenic. These discoveries of Kennaway and his colleagues

have led to an enormous world-wide activity in this field of cancer research. Large numbers of carcinogenic substances have been prepared in the chemical laboratories, some highly active and some of low activity: most of them display their activity when painted on the skin or injected under the skin, but some induce cancer of the liver when fed to appropriate animals. In all, more than 200 such compounds have been obtained.

It has already been noted that carcinogenic properties depend upon the structure of the chemical compound. This was originally proved by Kennaway and Cook in their early work, removal of a methyl group from one place or addition of a group may diminish or even abolish or, on the other hand, may enhance the carcinogenic property of a substance. Structure and biological activity are thus closely associated, so far as any particular compound is concerned. There is a class of carcinogenic compounds, the phenanthrene group, which are related to one another chemically, and at the same time their skeleton structures are found in some substances which are natural products of the body. It once seemed to be a possibility that these facts might eventually lead to a generalization of far-reaching consequences, but now many compounds, including azo dyes and even simple alkalis and acids and sugar, not in the least related to phenanthrene derivatives, have been proved to have carcinogenic powers. Thus, in the end, it has been found that the most important element in the discovery of pure chemical carcinogens is that they provide the means by which the genesis of a tumour can be studied, both chemically and histologically.

To take the *histological investigations* first.—It has been shown in recent years by a number of investigators that the process of cancer induction is extremely complex. When a chemical carcinogenic agent is applied to the skin of man or mouse the earliest sign of its activity is the appearance of a papilloma, usually called a wart, the papillomas may occur in large numbers, especially on the rabbit, and from one or more of them the true cancer may later take origin. These benign growths have not hitherto attracted much interest, probably because they were regarded as merely representing a gradually heightened energy of cell proliferation brought about by the chemical substance, and partly because the true malignant cell is the ultimate object of research and study. Moreover, this way of looking at the induced warts is derived from an unexpressed belief that cancer is a final state which ensues from increased proliferation of cells, an extreme condition of cell life in which a new rhythm of division has become a fixed habit. Rous and Kidd (1941) investigated the nature of these warts and their relationship to the cancers which develop subsequently. They studied the warts which occur in rabbits after application of coal tar or a pure chemical carcinogen, and stated precisely what has been the experience of hundreds of other investigators, namely, that these benign local epidermal growths spring from a diffusely altered epidermis, that they enlarge by intrinsic cell proliferation, appear more or less abruptly, are autonomous in mode of growth, are independent, in MacCallum's words, "of the mechanical laws which govern the hereditary form of the body," and that they are useless to the rabbit. These are among the best criteria of new growths but, since they dwindle and disappear if tarring is stopped, it cannot be said that they are irreversibly different from normal epithelium. This is a characteristic of true

malignant new growths, and consequently it has been difficult to assign to warts an exact status in the neoplastic process. But it was pointed out by Rous that the conception of true neoplasms being endowed with perpetual powers of independent proliferation is derived from studies of the extreme stage of cancer, the clinical cases, and there may well be large numbers of latent cancers which never come under observation. Rous and his colleagues proved by a long series of careful experiments that when a carcinogenic substance is applied to the skin, more epidermal cells become neoplastic than ever declare themselves by forming tumours. These cells may remain latently neoplastic for long periods of time and then, when favourable conditions occur, may grow and become tumours. Hence a sharp distinction must be made between inception and formation of tumour, between factors which render cells neoplastic and factors which affect their subsequent behaviour. Most of the recognized carcinogens cause cells to become neoplastic and at the same time provide conditions which favour the formation of a tumour. The conditions which in life favour tumour formation are usually chronic inflammation and injury. There are substances which although not themselves carcinogenic do favour tumour formation. An example of such a substance is croton resin (Berenblum, 1941). The ability of neoplastic cells to lie latent and then quickly to become dangerous new growths may provide an explanation for some of the puzzling clinical instances in which a cancer appears to have been caused by injury.

Turning now to *biochemical investigations*, it might first be pointed out that immense efforts have been made to discover how the numerous and different remote causes of cancer—the chemicals, the radiations, and worms—act, and whether or not there is some common mode of action, if, for example, each sort of insult causes the formation in cells of a single type of chemical substance which possesses the real carcinogenic power. Variations on this theme are numerous, but so far no satisfactory solution to the problem has been found. The subject is complex, and rapid progress cannot be expected. But many interesting observations have been made and attractive hypotheses have been advanced. Among the observations the most interesting is that relating to the metabolism of sulphur as it affects the induction of tumours (Crabtree, 1944). It has been proved that non-carcinogenic compounds—bromobenzene, for example—which specifically lower sulphur metabolism in cells, cause a retardation, or even, in certain conditions, a reversal of the carcinogenic action of 3,4-benzpyrene. Other compounds known to interfere with other specialized metabolic processes have a negligible effect on the initial stages of carcinogenesis. At present it would appear to be necessary to postulate a direct reaction between the chemical carcinogen and sulphur compounds present in the cell to explain the inhibitory activity of bromobenzene and such-like substances.

The most attractive hypothesis advanced by the biochemists to explain both the process of tumour induction and the continuation of cancer cells as independent autonomous growths is as follows—It is assumed that the primary phase of carcinogenesis is a coupling of the chemical compound with a protein—probably a nucleo-protein—leading to the emergence of an “altered protein,” enzymic in nature, self-duplicating and capable of provoking the cell to proliferate inde-

pendently No evidence has been found to support the hypothesis which is, in fact, an attempt to reconcile the apparent conflict between tumours which are known to be caused by a virus and tumours from which no active virus can be extracted There are better explanations of the difficulties than this hypothesis offers, and these will now be given

THE PROXIMATE OR INTRACELLULAR CAUSE OF CANCER

There is a theory that cancer cells are mutants of normal cells and that the power to proliferate autonomously, independently of body needs, is merely an expression of the mutation There is no evidence to support the theory, and quite obviously it is merely using a word as an explanation of facts The analogies—such as are found in the somatic changes in plants and insects, the spray of delphinium with white flowers, the rest being blue, or the fern found with a ruffled pinna, and so on—are more deceptive than analogies usually are Moreover, a close study of the genesis of a cancer has proved that not one, but many, mutations would have to be postulated to account for cancer And this leads to more difficulties than the original problem presents All discussion of papers and theories on this aspect of cancer will therefore be neglected

The virus factor—So far the only proximate cause for which there is evidence is a virus In 1911, Peyton Rous demonstrated that a sarcoma of the domestic hen can be propagated by injection of a cell-free filtrate The agent in the filtrate comes from the tumour cells and possesses all the properties by which a virus is described The differences in action between a virus and a chemical carcinogenic substance are that viruses act at once and specifically, causing tumours to appear in a few days, and always tumours of the same sort as that from which the virus was obtained, that they increase in quantity *pari passu* with the growth of the tumour, thus proving that they multiply in the tumour cells, and that they act as antigens provoking the formation of antibodies The remote causes of cancer, the chemical and physical agents, do none of these things, they must act a long time to cause tumour formation, they do not multiply, and they do not cause antibodies against themselves to appear The viruses are the true causes of the tumours in which they are found, but since active viruses are found in only a small percentage of tumours available for study it is not surprising that the majority of workers have hitherto tended to neglect their investigation

One of the most important recent discoveries was made by R. E. Shope (1933), who found a wild rabbit suffering from a papilloma of the skin He proved that this papilloma is transmissible with cell-free filtrates, the shaved skin of a wild rabbit is scarified and filtrate is rubbed on to the scarified area Papillomas appear in a week or ten days and these can again be propagated in the same way The papilloma is an autonomous growth but is not clinically malignant, it does not give rise to metastases and therefore does not kill the rabbit, unless by mere massiveness and infection But it was found that when a tame domestic rabbit is used, papillomas form and these later, after months, become transformed into a squamous carcinoma, which metastasizes and kills the host (Rous and Beard, 1935) This is the first

instance of a mammalian tumour transmissible with cell-free filtrates, that is to say, a mammalian tumour with a demonstrable virus cause

Cancer research is a succession of dilemmas. The papilloma yields an active virus and the virus can start a fresh papilloma, if the papilloma is allowed to persist it becomes a true epithelioma. It would be expected that the active virus could be obtained from the epithelioma, but this is not so. All attempts to extract a virus from the skin cancer have failed, and it is necessary to resort to indirect and circumstantial evidence. This evidence may be as good as the best circumstantial evidence—as good as the logician's proof that the milk has been watered by finding a trout in it!—but in cancer it is not readily accepted because of the primary difficulty of conceiving a virus as a cause. Peyton Rous has been successful in transplanting the squamous carcinoma in rabbits, the number of successive generations now exceeding twenty, the rabbits in which the tumour grows invariably develop an immune body which neutralizes the papilloma virus. It can therefore be said that although active virus cannot be extracted from the epithelioma, it is nevertheless there, although the proof of its presence is indirect.

A similar phenomenon is met with in chemically induced sarcomas of chickens. These tar or dibenzanthracene tumours of chickens cannot be propagated with cell-free filtrates, but the blood serum of chickens in which these tumours grow for a long time acquires the power to neutralize active viruses derived from well-known strains of chicken cancers, such as the Rous tumour no. 1, the Mill Hill endothelioma, and the Mill Hill sarcoma of striped muscle. This again is an indirect proof of the presence of a virus in the chemical tumour, although direct transmission is impossible.

The general principle which emerges from these recent special instances, and which has been proved for the mass of chicken tumours which are propagable by direct injection of active virus derived from a tumour, is that the virus itself is inactive, or non-infective, and that it causes tumour formation only under special conditions. This principle has been recently demonstrated most strikingly by Bittner, in his work on mammary cancer in mice.

HEREDITY AND HORMONES

Bittner's discovery of what is now universally called *the milk factor* of mammary cancer was the culmination of a long series of researches begun by J. A. Murray (1911) in the laboratories of the Imperial Cancer Research Fund, and continued in the United States of America by Leo Loeb, Maud Slye, C. C. Little and many others, and in Holland by Korteweg. None of the researches was directed to the purpose of finding out if mother's milk has any influence on the genesis of mammary cancer; each was concerned with a limited objective and was stimulated by scientific curiosity. Murray in his investigation asked himself the question—"Is there any hereditary influence operating in the causation of cancer of the breast"? He had proved by experience that a small percentage of breast cancer occurs in any group of mixed stock mice, just as it is known that a comparatively small percentage of women develop cancer. The disease appeared mysteriously and apparently causelessly. Murray took early cases of cancer, excised the primary tumour and bred

from the cured mice. He found, after years of painstaking investigation, that female mice with a cancerous ancestry were three times as liable to cancer of the breast as mice whose mothers and grandmothers were known to have been exempt from the disease. The increased liability to mammary cancer was present in all age-periods, from three months to two-and-a-half years, which is the normal span of life in mice. The work was continued in America along the newly developed lines of genetic research. By means of brother-sister matings it is possible to breed out pure homozygous strains of mice, and likewise to perpetuate any given quality, such as colour of hair. By this process of breeding it was found possible to obtain strains of mice of which more than 90 per cent. of the females developed and died of mammary cancer, and strains in which mammary cancer was very rare, e.g., fewer than 1 in 500. The strains are known respectively as high or low cancer strains. From all this it once appeared to be true that heredity is the principal, if not the sole, cause of cancer.

The hormonal factor—In 1916, however, Lathrop and Loeb, in a highly original paper, proved that ovariectomy of very young females of a high cancer strain prevented the occurrence of mammary cancer, and later it was proved that when the excised ovaries are implanted in the brothers of the ovariectomized mice—in which they survive because of the homozygous character of the strain—the males often develop cancer of the breast. This work was carried out long before the ovarian hormone, œstrone, had been discovered, but Loeb drew the right, if cautious, conclusion from his experiments, namely that cancer of the breast depends, at least partly, upon the action of œstrin on the mammary epithelium. Hence two causes of cancer of the breast are now recognized, an hormonal and an hereditary influence. Years later Lacassagne, working in Paris, proved that administration of folliculin subcutaneously in males of the R 111 Paris high cancer strain of mice induced cancer readily. This was a complete confirmation of Loeb's conclusions.

It has now been proved conclusively by a host of workers that cancer of the breast can be started by treating males with œstrin. The inbred high cancer strains vary somewhat in the extent of response, the R 111 strain reacting most readily of all. But it has also been proved that pure-bred strains, the females of which are not liable to develop cancer, do not respond at all to œstrinization. Mixed stocks which normally show a low percentage of breast cancer respond slightly. There is a parallel between the natural liability to cancer of the breast and cancer response to treatment with œstrin.

The next step in the research was made by geneticists, who naturally in their investigations cross-bred mice of high and low strains. It was found that when the mother was of a high and the father of a low cancer line, the hybrids developed cancer to the same extent as the high line from which the mother was derived, conversely, when the mother came from a low cancer line the hybrids showed no cancer. It thus appeared that cancer heredity was sex linked. Bittner's discovery (1939) was made in researches designed to find an explanation of this strange phenomenon in which it appeared that Mendelian laws were crumbling. He removed the new-born mice of a high cancer strain as soon as possible after birth and fostered them on mothers of a low cancer strain, the reverse experiment was!

also made, new-born mice of a low cancer strain being fostered by high cancer strain females. It was found that females of a high cancer strain which had not been permitted to drink their own mothers' milk did not develop cancer later in life, and, conversely, about 20 per cent. of females of strains which very rarely die of cancer and which have drunk the milk of high cancer strain mothers, die of mammary cancer in middle and old age. All these experiments have been confirmed again and again.

It thus becomes plain that cancer of the breast in these inbred strains, in which most or all of the accidental conflicting variables have been eliminated, depends upon the simultaneous cooperation of three factors—an inheritable tendency to mammary cancer, an hormonal influence, and a factor present in mother's milk. The complexity of cancer causation is well illustrated by this long international piece of research.

It is not possible to describe in detail all the work which has been done to elucidate the nature of the milk factor. The simplest and most direct interpretation of the results so far obtained is that it is a virus. The factor can be obtained directly from the tumours which it participates in starting. It passes from one generation of mice to another and therefore multiplies. Its size is uniform and is about $70\mu\mu$. The factor can be obtained from the blood of mice, both male and female, of the high cancer lines, and from internal organs such as the spleen and thymus gland, it is therefore widely distributed throughout the body. By injecting animals with the milk factor a neutralizing antibody can be obtained.

If the "milk factor" is eventually proved to be a virus then it should be noted that its properties regarding infectivity are in harmony with all the information available concerning viruses in other animal tumours. Alone it is incapable of acting pathogenically. Conditions must be just right and the complexity of these conditions is difficult to unravel. Further, it must be emphasized that the virus is once again playing the part of the proximate cause of cancer, the hormone and heredity being predisposing or remote causes.

It can readily be seen that cancer investigations are now rapidly approaching the stage at which all the apparent conflicts between chemical and physical, genetic and virus elements in causation are becoming reconciled.

References

- Berenblum, I (1941) *Cancer Research*, 1, 44.
Bittner, J J (1939) *Amer J Cancer*, 36, 44.
Crabtree, H G (1944) *Cancer Research*, 4, 688.
Lathrop, A E C, and Loeb, L (1916) *J Cancer Res*, 1, 1.
Mackenzie, I, and Rous, P (1941) *J exp Med*, 73, 391.
Murray, J A. (1911) *Imp Can Res Fund*, 4th Sci Rep.
Rous, P, and Beard, J W (1935) *J exp Med*, 62, 523.
—, and Kidd, J G (1941) *Ibid*, 73, 365.
Shope, R E (1933) *Ibid*, 58, 607.

THE SURGICAL TREATMENT OF MALIGNANT DISEASE

BY AIR VICE-MARSHAL GEOFFREY KEYNES, M D , F R C S

*Surgeon, St Bartholomew's Hospital, Mount Vernon Hospital, and Radium Institute,
Senior Consultant in Surgery to the Royal Air Force*

TWENTY-FIVE years ago it would have been possible to write of the surgical treatment of malignant disease almost without reference to any alternative method. To-day the balance is profoundly altered, and the time is past when any surgeon should treat any form of malignant disease without first asking himself whether the patient might not benefit more by radiotherapeutic treatment instead of, or in combination with, surgery. It begins also to be advisable to consider the possibilities of biochemical treatment. The responsibility of the surgeon has therefore increased in that he may have to call in the aid of a team of experts, since it will be clearly the province of the surgeon to know his own limitations rather than of the general practitioner to make the decision in favour of one form of treatment or another. The present article therefore has to be a survey of how much of the field of treatment of malignant disease remains for the surgeon, and must suggest where the demarcations of this field are found to lie at the moment. But change is constantly taking place, and will soon be moving faster when the present pre-occupation with the problems of traumatic surgery have become less insistent.

CANCER OF THE BREAST

Discussion may suitably begin with one of the most common forms of malignant disease—carcinoma of the breast—a particularly relevant subject because it is here that surgery has found one of its most encouraging lines of advance. It is many years since the so-called "radical" operation became established in general favour, and it has indeed been so firmly established that it has been subject to modification far more slowly than its defects have really demanded. This has been due partly to the relative accessibility of the primary and some of the secondary disease, so that the surgeon is able to perform an operation that is satisfying in its apparent completeness. Having done it, his conscience is at rest, a clean sweep, based (it was believed) on anatomical knowledge, has been made, surgical pride has been flattered by a precise and rapid dissection. Statistics have shown a gratifyingly high proportion of five-year survivals—provided strict selection has isolated the group of patients in stage I of the disease—so that the eye could rest on a high figure, 60 or 70 per cent., before it passed quickly over the rather distressingly low figures for stages II and III. Statistics, however, have usually ignored the large percentage of patients among the survivors with a disabling œdema of the arm due to the very thoroughness of the dissection. It has also ignored the high incidence of patients in stages II and III who have broken out in a rash of local

recurrences within a few months of the operation, and there has been but little tendency to ask the pertinent question if these recurrences may not in many instances have been actually caused by the operation. Surgical complacency has been, indeed, hard to shake, and far too slowly has the view gained ground that if radiotherapy were given its proper place in treating every patient with carcinoma of the breast, then might the rather barbaric "radical" operation be frequently modified in favour of non-conservative procedures, or even abandoned altogether.

Gradually, however, a large body of evidence has accumulated to show that radical surgery alone is incapable of giving the best results and that irradiation with high-voltage X-rays or radium is an essential part of the treatment. In one district of Scotland the radical operation has in fact been virtually abandoned for several years past in favour of local removal of the breast, or of local removal together with the lower axillary glands when these were obviously enlarged, this conservative operation being followed by irradiation. The results, hitherto unpublished, are showing better figures in the treatment of the disease as a whole than have ever been obtained before. It may be confidently predicted that a movement will take place towards conservative breast surgery, although the rapidity of the move will necessarily be conditioned by the time taken to implement the Cancer Act by the proper provision of centres where every patient can receive expert treatment by irradiation.

CANCER OF THE TONGUE

A somewhat similar story could be told of the treatment of carcinoma of the tongue, although here the position has been more thoroughly adjusted to the facts. No-one derived any sort of satisfaction from performing excision of the whole or a part of the tongue, and the results were deplorable, so that surgery has largely given way to irradiation by radium in treating the primary growth. On the other hand, the lymphatic drainage area has not proved particularly amenable to irradiation, and it is still agreed that block dissection of the neck is the best method of treatment. Here surgical craft can claim to be of paramount importance, for the operation must be a study in anatomical dissection if it is to be effective.

CANCER OF THE ALIMENTARY TRACT

In treating carcinoma of the breast and of the tongue the general surgeon must collaborate with the radiotherapist, but for almost the whole of the alimentary tract below the tongue, surgery still remains supreme. *Carcinoma of the œsophagus* has never been more than palliated by irradiation, whereas instances of brilliant success following various operations for extirpation of the growth are multiplying. These operations demand courage and ingenuity for their performance, and are never likely to be widely practised—partly, perhaps, because suitable material is uncommon, early diagnosis being still the exception rather than the rule.

The treatment of *carcinoma of the stomach* suffers from the same primary handicap, the majority of the lesions being already inoperable by the time they reach the surgeon's hands. Nevertheless, it is only the surgeon who can help the patient by either palliative or radical treatment, and as the operation of partial gastrectomy

becomes more widely recognized as the safe and satisfactory operation that it undoubtedly is, so will more gastric carcinomas, diagnosed perhaps as simple ulcers come to early operation. The gastroscopist meanwhile is doing his best to acquire experience wide enough to make himself a valuable agent in arriving at an accurate diagnosis.

Carcinoma of the large intestine again remains a field for pure surgery, and the principles of its treatment have not changed in any fundamental respect for many years. Many surgeons still like to mobilize a carcinoma of the large intestine, so that it can be brought outside the abdomen, and to form a spur on the Mickulic principle, which can afterwards be crushed to restore the continuity of the lumen. Others believe that an immediate end-to-end anastomosis of the large intestine with or without a preliminary cæcostomy, is, with the aid of chemotherapy and modern technique, not so dangerous as it has been painted, and so manage to save the patient a considerable period of convalescence.

The abdomino-perineal operation for *carcinoma of the rectum* was tending to become perineo-abdominal until the recent move in favour of simultaneous performance of the abdominal and the perineal parts of the operation by two surgeons. It is hoped that this innovation will make still safer an operation which was already surprisingly safe, considering its magnitude. There is also a wide field for the lesser operation of perineal excision of the rectum and it is greatly to be hoped that the possibilities of conservative resection of the rectum, keeping the function of the anal canal and sphincters intact, will be more and more exploited. Advances in the control of sepsis by means of the sulphonamide drugs are likely to help in the success of this kind of operation, since they can be used for bacteriostatic purposes, both inside the gut before operation and in the pelvis afterwards.

Although all the growths derived from the columnar cells of the intestinal mucosa are relatively so insensitive to irradiation, once the dividing line is passed at the anal margin the surgeon has to retire in favour of his colleague, for the squamous-cell carcinoma of the anal margin is one of the most radio-sensitive growths that occur anywhere. It can be readily cured by radium or X-rays, and should never be interfered with surgically, except to obtain a specimen for microscopic examination, since the treatment depends entirely upon the histological diagnosis.

Malignant neoplasms of the secreting glands remain on the whole the province of the surgeon. Salivary carcinoma is extremely insensitive to irradiation, and must be extirpated as completely as possible by operation.

THE PANCREAS AND GALL-BLADDER

Carcinoma of the pancreas is completely insensitive, but it is also seldom amenable to surgery, although one or two successful removals have been recorded.

Carcinoma of the gall-bladder region is also insensitive and is usually inoperable. On the other hand, a malignant growth of the ampulla of Vater, producing biliary obstruction, can, not infrequently, be extirpated with success, and any surgeon who aspires to proficiency in gall-bladder surgery must be prepared to perform, without notice, a transduodenal resection of the common bile duct, with restoration of biliary continuity by some means or other.

DUCTLESS GLANDS

Among the ductless glands, the *thyroid* demands urgent surgery, by which means as complete a removal of the growth as is possible should be done. If some residua of growth remain attached to the larynx or trachea, no serious risks need be taken in an attempt to remove them, for these will respond well to deep X-ray therapy, which should always be given after surgery has done its utmost. After the combined treatment an excellent prognosis can often be given.

Carcinoma of the thymus gland, producing myasthenia gravis, has recently come within the range of surgery, provided the growth has not begun to infiltrate the lung and other structures. It is improbable that radiotherapy will offer a hopeful alternative.

CANCER OF THE LUNG

Carcinoma of the lung itself is now one of the recognized fields for the thoracic surgeon who is rapidly advancing the safety and scope of his specialty. Irradiation has seldom done more than palliate this highly fatal form of growth.

THE GENITO-URINARY SYSTEM

The *genital organs* are the usual sites of malignant teratomas, the ovary producing alternatively a papilliferous cyst, which may be malignant, and the testicle a seminoma, always a highly malignant form of growth. For all these the rôle of surgery is limited to removal, so far as is possible, of the primary growth. In the ovary this may or may not be complete, in the testicle it is usually extremely simple, the vas deferens and cord being excised also for as far as can be reached. It then remains for irradiation of the lumbar glands to complete the treatment in places where surgery cannot follow.

Carcinoma of the bladder remains an unsatisfactory field for any sort of treatment. Irradiation has been disappointing, but the results of partial or total cystectomy with implantation of the ureters in the rectum have not justified any enthusiasm for surgery. The best method of attacking carcinoma of the bladder is by early diagnosis while the disease is still in the pre-cancerous stage and amenable to surgical diathermy.

Carcinoma of the prostate gland has been in the same, or even a worse, position, and both surgeon and radiotherapist can welcome the better results that have followed the use of stilbæstrol by the mouth, even though this can only claim to be a palliative form of treatment.

Among the specialties, *carcinoma of the cervix* has provided a battleground for surgeon and radiotherapeutist, where both have claimed the laurels. It has, however, now become a losing battle for the surgeon, and there seems little doubt that the future lies with irradiation, so that Wertheim's operation will be performed with decreasing frequency.

CANCER OF THE LARYNX

In another specialty the surgical treatment of intrinsic carcinoma of the larynx was at one time highly developed, and heroic operations for radical excision of the

growth met with a surprising measure of success in the hands of a few experts. Then came the phase of surgery of access, in which fenestration of the larynx for the application of radium directly to the lesion tended to replace the more mutilating operations for removal. This in its turn seems destined to give way to some extent to pure radiotherapy, although variations in the sensitivity of the growth to irradiation still demand that surgical technique should be kept bright and keen so that it may be applied with adequate skill to those patients who need it. Here, as in so many other regions, collaboration by experts is the prime necessity.

CANCER OF THE SKIN

Carcinomas of the skin, including the basal-celled growth known as "rodent ulcer", which does not metastasize, are mostly radio-sensitive, and surgical interference is unnecessary. Excision, it is true, may be quite successful, but it has to be carried well wide of the disease and this may necessitate extensive and ingenious manipulation of the surrounding skin in order to close the gap without tension. An apparently simple operation may turn into a difficult problem of repair, which can only be properly solved after some training in the principles of plastic surgery. All this can be eliminated by the proper use of radium.

SECONDARY CANCER

The treatment of secondary disease is almost a subject by itself, and one that usually gets but little attention. It is, however, plain at the outset that most secondary carcinomas are for the radiotherapist rather than for the surgeon. The first example that comes to mind is secondary carcinoma of the breast. Here, *local recurrences*, if detected soon enough, can sometimes be removed by surgery, and thus may indeed be the only possible method of attack, the maximum dose of irradiation that the skin will stand having already been given. This self-limiting factor in radiotherapy is not an argument in favour of omitting it, the gain by its use being on the whole much greater than the loss, but even when it has failed to the extent of not preventing a local recurrence, it is likely to have limited the growth, so that excision may successfully eradicate it. The same principle may apply to external recurrences of other forms of malignant disease, and careful consideration should always be given to the possibilities of surgical treatment before pronouncing a verdict of "no further treatment possible."

The *skeletal metastases* that so often follow various cancers, particularly those in the breast, are, naturally, never amenable to surgery. They often, however, respond so well to high voltage X-ray therapy that life may be prolonged for years by its boldly judicious application.

SARCOMAS

So far only neoplasms of epithelial origin have been considered, and it is plain that there is here still a large field of activity for the surgeon. In treating malignant tumours of connective tissue, on the other hand, the surgeon tends now to take a secondary position. It is true that he may sometimes still be called upon to perform some of his most prodigious feats, such as amputations of the fore- or hind-quarter,

but even these will probably succeed a course of treatment by radiotherapy. It is now the accepted principle that even the most straightforward amputation of a limb for osteogenic sarcoma should be preceded by a full course of deep X-ray therapy, the survival rate having been shown to be appreciably improved by this combined method of attack. A neoplasm, however, such as an *osteochondroma*, which may form a massive tumour in some part of the pelvic girdle, is almost completely insensitive to irradiation, and so may provide material for a surgical *tour-de-force*. With the aid of blood transfusions and improved methods of anaesthesia, the patient's prospects of survival may fully justify his submitting himself to the hands of a carefully chosen master of the craft of surgery.

Other mesodermal tumours, such as *lymphosarcoma* or *multiple myelomas*, are wholly outside the range of surgical attack, and even a semi-malignant tumour, such as an *osteoclastoma*, is beginning to yield to radiological treatment, so that the surgeon may soon be eliminated, whether for conservative treatment by scraping or for amputation. Rarer tumours, such as *fibrosarcoma* or *myosarcoma*, which do not stultify all attempted treatment by rapid dissemination, can sometimes be successfully removed, since their positions may favour radical excision carried out with boldness tempered by good judgement. Most of these growths are not sufficiently sensitive to irradiation for any reliance to be placed upon non-surgical treatment.

The treatment of another neoplasm of intermediate type, the so-called *melanotic sarcoma*, or *carcinoma*, according to pathological taste, is still mainly surgical. Neither primary growth nor glandular metastases are sufficiently radio-sensitive to justify the omission of surgical extirpation as complete as it can be made. A common site for the primary growth is somewhere on the lower limb, and here it can be widely excised, the operation being followed by a block dissection of the lymph glands in Scarpa's triangle, whether secondary growth can be detected or not. This may be followed by irradiation with X-rays or radium—perhaps an act of faith, although one that cannot be omitted in the present state of knowledge.

CONCLUSION

It will be seen from this brief survey of the rôle of surgery in the treatment of malignant disease that its function is undergoing a progressive restriction. Only with great difficulty can fresh fields for surgery be opened up, whereas radiotherapy advances steadily, with almost unexplored possibilities still in view. On a superficial view it might be hoped that the ultimate goal would be the complete elimination of "the knife," the assumption being that this would minimize the patient's suffering. But nothing could be further from the truth. A clean surgical operation frequently entails much less severe, and much less prolonged, suffering than is caused by efficient irradiation. Indeed, if it were only considerations of pain and discomfort to the patient that decided the issue, then surgery would be more often the treatment of choice. But it is primarily cure of the disease that is held in view, and so the best of both methods must be used with balanced judgement. From either point of view it is still early diagnosis that influences, more than anything else, the ultimate results of treatment.

RADIOTHERAPY IN THE TREATMENT OF MALIGNANT DISEASE

By D W SMITHERS, M D , D M R

Director of the Radiotherapy Department, Royal Cancer Hospital (Free)

AND W V MAYNEORD, D Sc , F INST P

Director of the Physics Department, Royal Cancer Hospital (Free)

THE year 1945 marks the fiftieth anniversary of the discovery of X-rays by Röntgen, an event of tremendous moment in the history of pure science and medicine. During these fifty years many thousands of investigations have been made into the fundamental nature of the rays and their actions on living tissues with the consequent development of a scientific background for the clinical application of the rays in therapy and diagnosis.

One of the earliest results of the search for ways of producing X-rays was the discovery in the following year (1896) of radio-activity, and two years later of radium itself, followed quickly by the observation that the new rays were destructive of living tissues and might therefore be used therapeutically. For technical reasons the two subjects of X-ray and radium therapy developed separately and to some extent divergently, but during the last few years, thanks to the introduction of common methods of measuring the "dose" of X-rays and of the rays from radium, X-ray and radium therapy are now seen as two aspects of the same subject, and will here be treated as such.

PHYSICAL PRINCIPLES OF RADIATION THERAPY

Amid all the complexities of the biological actions of the radiations it soon became clear that these effects depended largely upon the amount of radiation given, the destructive biological effect increasing with the dose. It was natural therefore that the development should take its course towards more powerful sources of radiation and rays of greater penetration, so as to increase the tumour dose and make possible the treatment of more deeply seated lesions. Inevitably, too, the question of estimation of dose became the chief preoccupation of those concerned with the more physical aspects of radiation therapy.

In the early days, the successful treatment of cancer by radiation was necessarily confined to accessible tumours, and it must be confessed that this is still the chief field in which the radiation is curative.

Inasmuch as X-rays are normally more penetrating the higher the voltage at which they are generated, the methods of production of high voltages and corresponding X-ray tubes to withstand the electrical pressures have progressed until the few thousand volts originally used by Röntgen have been raised to one or even two million volts, whilst at present unorthodox technical equipment is raising the limit to twenty or even to one hundred million volts. Correspondingly on the radium side the few milligrammes of radium originally used would now be regarded as totally inadequate in most cases, and in large radiation centres radium

units comprising five or ten grammes of radium are employed in clinical practice. Naturally, with such powerful weapons the greatest care has to be exercised, not only in respect of the patient, but also in the protection of the staff.

Although the increase in power of the technical weapons used in the treatment of deep-seated lesions has improved the results obtained, it is necessary to beware of the conclusion that high voltage equipment alone is of use. It would be truer to say that a large radiation therapy centre requires equipment producing X-rays under a great variety of conditions and of different penetrations, for example, the type of apparatus employed for the treatment of skin tumours is not at all suitable for cancer of the lung or uterus.

It has been emphasized already that the biological effect of the radiation depends greatly upon the dose given to the tumour, and it was therefore an event of importance in the history of radiation therapy when in 1928 international agreement was reached on a unit of X-ray dose, the "röntgen". Subsequently, researches were carried out into the measurement of gamma rays (rays physically similar to X-rays and emitted by radium preparations) in the same international unit, and again provisional agreement on a unit of dose comprising both X and gamma rays was reached just before the war (1937). Since that time, experience of radiation therapy of a precision hitherto unknown has accumulated in a number of centres.

Using the new unit of dose, measurements of the dose received at a depth in the patient under a wide range of X-ray conditions have been made, and the X-ray therapist has now a mass of reasonably accurate data to guide him in his choice of technical procedure. Correspondingly, on the radium side, measurements of the radiation in the neighbourhood of radium needles and tubes have transformed the theory of interstitial radium therapy, as well as the use of intracavitary radium applied to such sites as the cervix uteri. Mathematical investigations have provided a clue as to the proper positions and amounts of radium required to produce uniform or non-uniform doses throughout the mass of tissues to be irradiated, whilst corresponding developments in the physics of telerradium (the use of large quantities of radium at a distance from the skin in a method analogous to the use of X-rays) have provided knowledge as to the optimum directions in which to point the beams so as to produce the chief destructive effects where most required.

Oddly enough, radiation therapy has thus provided many interesting mathematical problems, and the physicist engaged in radiation therapy must now have at his disposal a range of instruments capable of dealing with the complex three-dimensional geometry and analysis with which he will certainly have to deal.

It must be noted that it is only by the closest possible collaboration between radiation therapist and physicist that progress to the present position has been made. Such cooperation is likely to be of more, rather than of less, importance in the future. One of the most efficient ways of bringing together these two groups of people with such different training, and therefore of outlook, lies in the physicist attending regularly at radiological clinics and seeing there the difference between a neat diagram of radiation fields and cancer in its anatomical and most "unmathematical" forms. The radiotherapist, on his part, finds that regular visits to an experimental laboratory are stimulating and chastening experiences. Although a great deal remains to be done, a stage has been reached

when radiation can be accurately measured and applied to the patient, but it is particularly in the clinical application of laboratory methods that the greatest development is still required

BIOLOGICAL PRINCIPLES OF RADIATION THERAPY

Having then developed and obtained control of a sharp therapeutic weapon, attention is being increasingly directed to the next stage, namely, the complex problem of investigating the biological effects of these radiations. Here, again, the simultaneous interest of many men of diverse outlook and training is required, particularly the cytologist and pathologist, who must now carry the matter further forward in their own respective fields

In studying the biological effects of radiations the radiotherapist is always concerned both with the effect on tumour cells and with the effect on the tumour bed. Much knowledge has been acquired about the effect of radiation on cells, and some of the nuclear mechanisms by which radiation effects are caused in single cells are already known. In malignant disease the problem is complicated by the fact that a tumour is composed of a mass of abnormal cells differing greatly both in development and activity and embedded in normal tissues whose response to treatment will materially affect the response of the tumour as a whole. This makes it particularly difficult to apply the evidence as to biological response obtained with isolated experimental material. It has long been recognized that the response of a tumour to irradiation depends nearly as much upon the site at which it occurs as upon its histological structure. A deep-seated tumour may appear to be more resistant to treatment than one of similar structure situated near the body surface because of the difficulties in localizing an effective dose to the tumour situated at a depth, but this is not the only difference, a squamous-cell carcinoma of the pinna, for instance, is often more difficult to eradicate than a similar tumour of the face, a tumour of the tongue than a tumour of the lip, a carcinoma in a small atrophic breast than a similar tumour in a large fatty breast.

Knowledge of tumour-bed response is growing, as well as knowledge of the importance of the distribution of dose in time as well as space. Some of the individual applications given during a course of treatment are at present wasted, and some may actually be harmful if they do more damage to the tumour bed than to the malignant cells. It is becoming more and more obvious that when tumour response is considered as a whole, the way the treatment is spread out is, within reasonable limits, as important as the actual dose of radiation given. This has been suspected for some time, but it was not until the amount of dose given to a tumour could be estimated with considerable accuracy that it became possible to compare the importance of variation of dose within the therapeutic range and the fractionation of dose in time. The two are clearly closely related, but there has been a natural tendency to concentrate on dose, or dose in a certain over-all time, rather than on the intervals between individual treatments. The words "radio-sensitive" and "radio-resistant" are acquiring a new meaning. They were originally applied to immediate clinical tumour response and bore little relationship to curability, tumours that were thought to be "radio-resistant" at one stage becoming "radio-sensitive" as improved methods of applying treatment were evolved, radio-sensitivity was related to histology with little emphasis on site or tumour-bed

response That the response of a tumour to treatment should depend upon its environment and the intervals between treatments, and not solely upon its histological structure and the dose given, constitutes a change of emphasis in outlook that leads to fertile speculation on many of the problems concerned with puzzling variations in radiotherapeutic response There has been too much concern with an attempt to find the magnitude of "cancericidal" or "cancer lethal" dose which has only to be delivered in a certain total time for success to be achieved with the majority of tumours of a given histological type It is perhaps odd that this doctrine, which ignores the importance of individual variation, has been so widely accepted It was, however, an advance on the practice, still not quite eliminated, of treating curable, early accessible cancer with inadequate doses repeated at long intervals, often over a number of years, until the patient could no longer be cured by any method

RESULTS OF TREATMENT

Radiotherapy is now well established, its field is becoming better defined, and is likely to expand as knowledge increases A few tables are included here to indicate the results of treatment now being obtained by irradiation There is every reason to expect that these will be improved still further in the future Radiotherapy plays the paramount part in the treatment of tumours of the skin (table 1), mouth (table 2), larynx (table 3), and cervix uteri (table 4), for which it is an efficient form of treatment in the early stages of the disease, jointly with surgery, it forms an equal partner in the treatment of cancer of the breast (table 5), again with considerable success, it struggles with cancer of the lung, œsophagus (table 6), brain, bone, and bladder, with an undercurrent of disappointment enlightened by an occasional brilliant success at some sites and a steady improvement in results at others, in much the same way as surgery has done, but with a considerable palliative value not possessed by most surgical techniques The stomach, rectum, and most other abdominal sites are still almost the exclusive province of the surgeon, although the use of very high voltages has brought about an advance even in these regions The radiotherapist treats the lymphadenopathies and leukæmias, with the certainty

TABLE I
RESULTS OF TREATMENT OF NEW CASES OF BASAL- AND SQUAMOUS-CELL CARCINOMA OF THE SKIN
TREATED BY X-RAYS AT THE ROYAL CANCER HOSPITAL, 1935-1940
(Smithers, 1945)

<i>Basal-cell carcinoma</i>						
	No of cases treated	No lost sight of	No died of intercurrent disease	No recurred	No symptom-free	Symptom-free rate
Patients treated more than 5 years ago	123	43	21	6	53	90 per cent 5 years
Patients treated more than 3 years ago	259	44	28	13	174	93 per cent 3 years
<i>Squamous-cell carcinoma</i>						
Stage 1	93	15	11	14	53	79 per cent 3 years
Stage 2	11	0	1	7	3	30 per cent 3 years
Stage 3	10	0	2	5	3	38 per cent. 3 years
TOTAL	114	15	14	26	59	69 per cent. 3 years

The number lost sight of is largely due to the dispersal of patients living in London during the war; the majority should be traced eventually

TABLE 2

RESULTS OF TREATMENT BY RADIUM FOR CANCER OF THE MOUTH AND LIP AT THE CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE, MANCHESTER, 1932-1933 (Paterson, 1939)

Stage	Year	No treated	Net survival rate (per cent)	
			3 years	5 years
1	1932	66	70	67
	1933	98	69	66
2	1932	62	50	43
	1933	64	36	24
3	1932	89	24	19
	1933	69	30	20
4	1932	38	5	3
	1933	44	7	5
TOTAL	1932	255	38	33
	1933	275	41	34

TABLE 3

RESULTS OF TREATMENT OF INTRINSIC CARCINOMA OF THE LARYNX BY TELERADIUM AT THE ROYAL CANCER HOSPITAL, 1933-1944 (Lederman, 1945)

Total cases	Material	Survivals	Disease present	Dead	
				Untraced	Intercurrent disease
54 All cases seen were treated	23 operable	18 8 5 years or more 1 3-4 years 3 2-3 years 2 1-2 years 4 <1 year	3	1	1
	19 inoperable	1 5 years +	15	3	—
	14 recurrent	5 1 5 years or more 3 <1 year (1 after laryngectomy) 1 <1 year (disease present)	8	—	1

TABLE 4

PRIMARY CASES OF CANCER OF THE CERVIX TREATED BY IRRADIATION AT THE MARIE CURIE HOSPITAL, LONDON
RESULTS AT THE END OF FIVE YEARS
(Hurdon, 1942)

Classification	No examined	No treated to end of 1933	Living at end of 5 years	Died of cancer*	Died of inter-current disease	Survival rate at end of five years per cent.	
						Relative	Absolute
Stage 1	40	40	32	6	2	80 0	80 0
Stage 2	174	174	107	65	2	61 5	61 5
Stage 3	455	455	143	308	4	31 4	31 4
Stage 4	167	138	10	127	1	7 2	6 0
TOTAL	836	807	292	506	9	36 2	34 9

* 12 cases lost to view are counted as having died of cancer

TABLE 5

COMPARISON OF RESULTS BETWEEN RADICAL SURGERY AND SURGERY PLUS POST-OPERATIVE RADIOTHERAPY IN CARCINOMA OF THE BREAST TREATED AT THE ROYAL INFIRMARY, EDINBURGH (McWhirter, 1943)

			No of cases			Percentage symptom-free		
			1 year	2 years	3 years	1 year	2 years	3 years
Glands histologically negative	Radical surgery	Symptom-free	65	53	42	82	68	57
		Total cases	79	78	74			
	Surgery + radiotherapy	Symptom-free	85	58	39	98	91	91
		Total cases	87	64	43			
Glands histologically involved	Radical surgery	Symptom-free	77	52	33	54	37	24
		Total cases	143	141	135			
	Surgery + radiotherapy	Symptom-free	160	85	50	81	56	50
		Total cases	197	151	100			

All cases stages 1, 2 and 3 with axillary glands histologically examined

TABLE 6

RESULTS OF TREATMENT OF CARCINOMA OF THE OESOPHAGUS BY X-RAYS AT THE ROYAL CANCER HOSPITAL, 1937-1939
(Smithers, 1943)

No of cases seen	No treated	No completed treatment	No alive 1 year	No alive 2 years	No alive 5 years
51	44	32	13	5	3

Microscopical confirmation was obtained in 27 of the 32 cases that completed treatment, in 10 out of the 13 alive at 1 year, in 4 of the 5 alive at 2 years, and in 2 of the 3 alive at 5 years

RECENT CHANGES IN MORTALITY AT ALL AGES

Some, at least, of this difficulty can be avoided if the trend of mortality be not pursued into too distant a past. Attention will therefore be confined here to the changes recorded between the two world wars. The relevant figures for total mortality from cancer are given in table 1, the rates being standardized and thus allowing for the changes that have taken place in the age constitution of the population.

TABLE 1
ENGLAND AND WALES STANDARDIZED DEATH RATES FROM CANCER PER MILLION LIVING

Years	Males		Females	
	Average annual rate	Percentage change	Average annual rate	Percentage change
1921-23	959	100	971	100
1924-26	1011	105	990	102
1927-29	1027	107	994	102
1930-32	1042	109	980	101
1933-35	1046	109	969	100
1936-38	1068	111	960	99

It will be seen that for men the recorded death rate has been slowly, but persistently, increasing. In the years just before the present war it was about 10 per cent higher than in 1921-23, and it does not appear that the maximum point on the curve has yet been reached. With women, on the other hand, there was only a small rise between 1921-23 and 1927-29 and since then the rate has declined so that in 1936-38 it was a fraction below the level of nearly twenty years earlier. (The trends for both sexes are very slightly affected by changes in the classification of causes of death between 1921-30 and 1931-38, but these changes are insufficient to alter the general picture.) These differing time sequences have led to one other change in the general picture of cancer mortality in this country. In the past the recorded mortality for women was invariably higher than that for men. Since 1924 the standardized mortality for men has been the greater.

RECENT CHANGES IN MORTALITY AT DIFFERENT AGES

Whilst these standardized rates give a simple and useful summary of the general trend of mortality, it is clearly of more importance to see what underlies them at different periods of life. The necessary figures are set out in table 2—

TABLE 2
ENGLAND AND WALES DEATH RATES FROM CANCER PER MILLION LIVING AT DIFFERENT AGES

Years	0—	25—	35—	45—	55—	65—	75—	85 +
<i>Males</i>								
1921-30	33	115	416	1629	4768	9405	12677	12300
1931-35	35	119	440	1628	4693	10144	14266	13619
1936-38	40	145	462	1624	4705	10195	15121	14290
<i>Females</i>								
1921-30	27	159	762	2150	4281	7548	10877	12016
1931-35	29	158	731	2081	4107	7545	11453	13407
1936-38	32	159	712	2033	4017	7452	11613	14738

With men the registered mortality has risen at the two ends of the age scale, namely at ages under forty-five, when the death rate is at all times small, and at ages seventy-five and over, the time of life at which any tendency to an increasing accuracy of diagnosis and of certification of cause of death might well be at its highest. Another possible factor in an upward trend here would be the prolongation of life through modern methods of treatment and the consequent postponement of death until these later ages. At the important mid-ages, forty-five to sixty-five, there has been virtually no change in the death rate between the years 1921-30 and the last years before the war.

With women there has been a clear decline in mortality over the main span of life, namely between the ages of thirty-five and seventy-five, and an increase only at the highest ages of seventy-five and over—and possibly in the very low rate at ages under twenty-five.

Between the sexes the main contrast lies in the greater mortality in women between the ages of twenty-five and fifty-five, which is mainly due to the special frequency at this time of life of cancer of the uterus and breast.

CHANGES IN MORTALITY OF THE MAIN SITES

These total cancer mortality rates, whether standardized or at specific periods of life, represent the summation of the figures for different parts of the body. It is of interest to inquire how far those separate site rates have varied in recent years and what contributions each has made to the total. The principal data for the inter-war years are briefly shown in table 3, page 30.

For men, it will be seen, there has been a distinct fall in the recorded mortality for cancer of the lip, tongue, jaw, œsophagus, liver, and for rodent ulcer, and a distinct rise for cancer of the intestine, pancreas, prostate, and particularly the lung. For women the improvement is marked in cancer of the uterus and liver; their increases lie in the intestine, ovary and Fallopian tube, pancreas and lung.

The apparent decline in some of the internal sites, for example the liver, may without any doubt be attributed to the more accurate certification to-day of the primary site of the growth. The same factor must inevitably lead to increases in the other sites which are recognized more frequently as those primarily affected. Such transferences may well account for the recorded increase in cancers of the stomach, the intestines and the pancreas. On the other hand, the improvement in such external sites as the lip, tongue, jaw, penis and scrotum, and rodent ulcer, indicates a real declining incidence together, perhaps, with more effective treatment of these forms.

The large increase in cancer of the lung suggests by its very rapidity and magnitude that improved methods of diagnosis are partially responsible. But some real increase seems likely, and the greater rise in men than in women is a noticeable feature of its trend.

GEOGRAPHICAL VARIATIONS IN MORTALITY

Similar difficulties of interpretation and uncertainty as to the uniformity in accuracy of diagnosis have also in the past stood in the way of studies of local differences in cancer mortality. With generally improving standards, however, statistical

analysis for recent years becomes worth while, and may point the way to problems requiring explanation. Valuable analyses of this kind have been made by Stocks (1936, 1939) for the years 1921-30 and carried to a later date in the Registrar-General's reports (R.G. 1937). Wide geographical variations in the recorded mortality are apparent in the earlier decade. For example, cancer of the œsophagus in men showed a region of relatively high mortality in the south-east quadrant of England, and particularly in an area north of the Thames, comprising the counties of Warwick, Oxford, Berkshire, Buckingham, Middlesex, London, Essex and West Suffolk. Rectal cancer gave a somewhat similar picture, so that the responsible factors, whatever they may be, seem to affect both these sites.

Mortality from cancer of the stomach was strikingly high in Wales for both sexes, particularly in its northern counties, and this excess persisted in 1937. It does not seem reasonable to explain this entirely in terms of diagnosis and accuracy of death certification and, since the north-western areas of England likewise tend to show high rates, it cannot be readily interpreted as a racial characteristic. It is possible, Stocks suggests, that dietary habits are a factor and specific investigation might repay the effort.

With the two important sites in women, the breast and the uterus, there were also in 1921-30 considerable local differences. The former showed in general a rather higher rate in the urban than in the rural parts of the country and a relatively low incidence in the Welsh counties. Cancer of the uterus revealed a still more distinct excess in the towns and had, at ages twenty-five to sixty-five, a region of relatively high mortality in the north-easterly counties, from the Scottish border to Norfolk. These northern counties continued to show a marked excess in 1937, but the lowest rates for cancer of the breast and ovary. Variations in social class and in fertility would not fully account for this variation and other underlying causes must, it seems, have been operative. Cancer of the lung is of particular interest in view of its great recorded increase and large excess in males, as previously shown. Its registered mortality rises steeply with increasing urbanization but this is likely to be due in part to more efficient diagnosis. On the other hand, even if observation be limited to large cities with their less varying standards, there still remains much contrast to be explained. In general, it is clear that there exist wider differences in the geographical distribution of cancer mortality than can be readily dismissed as functions of accuracy of observation and reporting. They still await solution.

SOCIAL ASPECTS OF MORTALITY

One of the most interesting aspects of mortality from specific causes of death lies in their variation between one social class and another. Malignant disease is no exception. The latest available figures published by the Registrar-General relate to the three years 1930-32, the deaths in which can be related to the relevant populations recorded at the census of 1931 (R.G. 1938). In studying such occupational mortality rates, and their segregation into broad social classes, it is advisable to limit the observations mainly to the principal working years of life, twenty to sixty-five. At older ages the former occupation of the retired person tends to be omitted on the census return, so that no accurate population figure becomes available to relate to the previous occupations of the dead, which are generally included

on the death registration statement. At these ages, twenty to sixty-five, the simplest statement of the relative mortality experience of a group is its standardized mortality ratio. This figure takes into account the different age constitutions of the populations at risk, which may vary considerably between one occupation and another. In short, it compares the total registered deaths in a specific group, from all causes or from a particular cause, with those that would have occurred in it if at each age period it had experienced the corresponding rate for all males in England and Wales (or females as the case may be). The standardized mortality ratio is the percentage ratio of the deaths actually registered to the standard deaths as thus calculated, and its situation above or below 100 thus reveals whether the group in question has had a favourable or unfavourable mortality experience. The general picture for cancer of all sites is given in table 4.

TABLE 4
ENGLAND AND WALES STANDARDIZED MORTALITY RATIOS IN 1930-32 AT AGES 20-65

Social Class	Males		Married women	
	All causes of death	Cancer all sites	All causes of death	Cancer all sites
I Professional, etc.	90	83	81	96
II Intermediate between I and III	94	92	89	97
III Skilled workers	97	99	99	101
IV Intermediate between III and V	102	102	103	99
V Unskilled workers	111	115	113	106
All	100	100	100	100

For men, it will be seen, the social gradient in malignant disease is no less marked than that produced by all causes of death. The difference between those most and those least favourably situated, from the economic and environmental standpoints, is, in fact, rather wider. With married women, on the other hand, graded according to the social class of the husband, there is a similar trend to that shown by men for all causes of death, but relatively little variation in their incidence of fatal cancer, irrespective of sites. For the men, but not the women, it is possible to make a comparison of the social gradient in these years 1930-32 with that prevailing in 1921-23. In 1930-32 the ratios varied, table 4 shows, between 83 for class I and 115 for class V. In 1921-23 the corresponding figures were 80 and 123. With generally improving conditions of life this slight reduction in the contrasting levels may lie in a decrease in the intensity of the responsible irritant factors and, perhaps too, in the more effective treatment of some forms of cancer.

These total figures are, however, composed as usual of very varying components, and it is of still greater interest to study the contributions made to them by diseases of the different sites of the body. With men, such division reveals, the more pronounced rise in mortality with descent in the social scale is that associated with cancer of sites lying in the upper alimentary tract (the lip, tongue, mouth, throat, jaw, pharynx, rest of buccal cavity, œsophagus and stomach). In 1930-32 successive standardized mortality ratios for this group of sites were, at ages twenty to sixty-five, 63, 80, 97, 109 and 129 passing down from class I to class V. A trend similar to this is also apparent for married women (table 5).

1921-23
1930-32
1936-37

according to the social class of the husband) It therefore seems that the causative factors responsible for this class differentiation must lie, not so much in the specific occupations themselves, as represented in the social groups, as in the more general economic and environmental circumstances and habits of life which are associated with the occupations lower in the social scale A contrast to this, on the other hand, is shown by cancer of the larynx, which records a considerable social trend with men (in the same direction as the above) but no significant gradient for married women The sex difference suggests some hazards more specific to occupation Cancer of the skin also rises but does so for both sexes, so that here again rather more than a purely occupational risk seems to be concerned

With men there is no important site which shows the reverse relationship, namely a high rate in class I with a falling incidence to class V (except, perhaps, the mediastinum) With married women such a trend is pronounced for cancer of the breast and the ovary, whereas mortality from cancer of the uterus runs steeply upward from class I to class V Differences in fertility must contribute to these trends but seem insufficient to account for them entirely

Sites which reveal no clear relation between mortality and social class are mainly also deep-seated, and include the intestines, rectum, lung and, in men, the liver

a ra

relativ

a still

SOME OCCUPATIONAL CONTRASTS

a regio from these broad social groupings to the occupations allocated to them, Scotland Registrar-General's figures reveal many striking differences in mortality and, indeed, in some cases suggest unexpected and unidentified factors On the most favourable side of the picture lie the agriculturally employed—farmers, agricultural labourers, gardeners, and the like—and some of the professions For instance, for the former there were registered in 1930–32, 2,755 deaths from cancer of all sites at the working ages of twenty to sixty-five At the standard rates of all males there would have been 3,566, so that the actual experience was nearly 25 per cent better than the standard Their recorded deaths are especially low in cancer of the buccal cavity and pharynx and of the lung

In the professional groups, particularly favourable experiences are shown by clergymen, teachers, bank and insurance officials and medical men Here the observed deaths at ages twenty to sixty-five are, respectively, 56, 57, 69 and 70 per cent. of those expected of the standard rates

At the unfavourable end of the scale are included furnacemen, skilled gas workers, dock labourers and stevedores, drivers of horse transport, makers of alcoholic drinks, inn and hotel keepers, barmen and waiters Here the observed deaths are in each case between 40 and 60 per cent. in excess of the expectation of the standard rates, and the excess is usually spread over many sites The last-mentioned groups, with their obvious association with alcohol, are of interest. Analysis of their mortality by sites affected shows that the only non-contributors to the excess are the stomach and skin (and perhaps the large intestine), and that the principal contributors are the oesophagus, larynx and buccal cavity, although it is also apparent for the lung and rectum. The wives of men so employed may be noted, no significantly abnormal incidence of malignant disease

SUMMARY AND CONCLUSIONS

In spite of the difficulties and inevitable errors inherent in the study of any defined cause of death, it seems that in this country the level of mortality from malignant disease as a whole has shown no appreciable variation over, roughly, the last twenty years—when allowance has been made for the ageing of the population. It is probable that the death rate of men has continued to rise slightly, particularly at the most advanced ages, but with women the main span of life reveals a decreasing rate of mortality. There are indications that this improvement is likely to continue. The wide geographical, social and occupational contrasts, on the other hand, imply the presence of underlying etiological factors not yet identified, for it is impossible to believe that such differences are all merely functions of the accuracy of death registration. For example, facilities for better diagnosis would be likely to favour the higher social classes rather than the lower, and thus reduce rather than enhance the social gradient. It is also noticeable that this gradient is a feature of sites in which the diagnosis presents no serious difficulties. The valuable data relating to the wives of men in different occupational and social groups, first published by the Registrar-General for 1930–32, makes it clear that this social incidence is not a function of occupation in the narrow sense, but is likely to be a product of the broader economic and social environment, of association, perhaps, with other diseases, or of constitutional differences. With improving standards of life such contrasts may be expected to become less pronounced, but unfortunately the war has prevented the accumulation and publication of the relevant statistical data. On the other hand, there is no reasonable doubt that there exist also specific occupational hazards which await recognition. The identification of such risks is not simple, for the production of malignant disease is often long delayed, occupations change meanwhile and the original responsible factor consequently goes unrecognized.

In general, it seems that much malignant disease is preventable, using that word in its broadest sense, through communal or individual effort leading to the correction of unfavourable environments and habits of life, and to the early recognition and treatment of cases. Knowledge of the epidemiological characteristics of the disease is therefore of fundamental importance in pointing the way to possible factors in causation and in focusing attention upon the differential incidence which falls upon sections of the population. Such knowledge, however, rests upon the accuracy of diagnosis of the disease and of its primary site and upon the standard of certification of the causes of death. Although improvements in both must oft as already stressed, lead to serious difficulties in the interpretation of mortality differences, both in time and space, they can but give, in the long run, a clearer picture of the epidemiological setting. In the production of that clearer picture the medical practitioner has to play the principal part.

References

- Hill, A. Bradford (1942) "Principles of Medical Statistics," 3rd edition, London
 Registrar-General's Statistical Review (1937) Text
 ——— Decennial Supplement (1938) "England and Wales Occupational Mortality"
 Stocks, P (1936, 1939) *Ann Repts Brit Emp Cancer Campn*, London

THE MANAGEMENT OF ABORTION

By ANTHONY W. PURDIE, M.B., Ch.B., F.R.F.P.S., M.R.C.O.G.

Obstetric Surgeon, North Middlesex County Hospital

PAIN and hæmorrhage following a period of amenorrhœa are most likely to be due to abortion. Yet there are many mistakes in diagnosis. Therefore both the history and examination findings merit consideration.

DIAGNOSIS

The history, given by the patient, can be most helpful. She may say that she passed an object like a child, and that this was followed by a lump of fleshy stuff. If the story is true there would be no doubt that she had had an abortion. There are cases in which pelvic examination alone makes it impossible to differentiate between threatened and incomplete abortion. Here a reliable history of the passage of a fleshy lump or large clots of blood, even in the absence of the known passage of a fœtus, would indicate that the abortion was incomplete. On the other hand, a patient finding herself to be bleeding may hurry to the lavatory, and pass a lump which she flushes away without inspection. It may only have been blood clot and she may not even have been pregnant. Others can only give a confusing history, as pregnancy may have occurred after a period of menstrual irregularity or amenorrhœa.

In hospital, the woman who unwittingly misleads is sometimes seen. She states that she had a miscarriage on a certain date. Asked how she knows that, she replies "My doctor told me so." Further questioning reveals that the practitioner, hearing her story of passing blood and clots, admits that she might have had an early miscarriage, when in fact she was suffering from a functional uterine hæmorrhage.

Finally, there is the patient who hides the truth. She has attempted to procure an abortion or has had someone else do so. She may fear that if she tells the truth expectant treatment will be adopted, perhaps successfully, and she may yet have to bear the child of which she is so anxious to be rid. On the other hand she may be just afraid. She feels that she has done wrong. She is in pain, feeling very ill and appalled by the consequences of her acts. Perhaps, afraid of the police and publicity, she denies everything, sometimes even in the presence of obvious peritonitis, and trusts that the omniscient medical officer, whom she is attempting to deceive, will do what is best and make her well. The history, while at times distinctly helpful, may therefore have to be discarded and a diagnosis made on examination alone.

The typical findings are well known. Here, too, there are snags. The general

condition should first be considered. The effect of hæmorrhage may be obvious; the patient may be lying in a pool of blood. Pallor out of proportion to the amount of blood lost should raise the possibility of intraperitoneal bleeding. Reference will be made later to the importance of blood pressure readings.

The breast changes are of greatest value in a possible first pregnancy. In multiparæ, however, secretion is not conclusive proof of existing pregnancy, for it may be obtainable years after the pregnancy responsible for its initiation. Also, early abortion may occur before any breast signs have developed.

On abdominal examination, is the uterus in keeping with the patient's dates? If it is too large, multiple pregnancy, hydatidiform mole, and uterine fibroid with pregnancy should be considered. The fundal height may be greater than expected but the uterus, as a whole, not as bulky as a pregnant uterus normally is when reaching that height. It gives the impression of being perched on top of something below it. An ovarian cyst in the pouch of Douglas, considerable blood clot in the vagina, a loaded rectum or a full bladder, may produce this effect. If such possibilities are overlooked, wrong conclusions may be drawn.

Abdominal tenderness is not usually elicited unless directly over the uterus itself. It may be found, however, with slight recoil tenderness in the "peritonism" which accompanies some cases of inevitable abortion. It is also present with a variable amount of rigidity and recoil tenderness in abortion with peritonitis. In the latter the patient usually looks more ill and the pulse rate may be persistently faster.

The patient should pass urine before abdominal examination, because even a healthy subject experiences pain if the abdomen is pressed upon while the bladder is full.

Vaginal examination will then be made. For this the bladder *must* be empty. I have seen more mistakes made in pelvic examination from failure to observe this golden rule than from any other single factor. Sometimes an enema is required for accurate findings. While making the vaginal examination any blood clot present should be scooped out, for its presence in the vagina, in large amount, seems to interfere with the contractile power of the uterus and so permits bleeding to continue.

The fingers are swept round the vaginal wall to determine the presence of inflicted injury. Is the cervix closed or dilated? Can any tissue be felt protruding and if so what is its nature? In what direction does the cervix point? But the only sure way to decide whether the uterus is anteflexed or retroflexed is to feel the body of the uterus between the examining hands. The position, size, outline, consistence, and mobility of the uterus should be noted.

It is not necessary, or even desirable, to pass a vaginal speculum in all cases, but when the likely diagnosis is threatened abortion it should be done. This will ensure that a mucous polyp of the cervix, which may cause slight or irregular bleeding, and which even experienced fingers may fail to detect, is not overlooked. Patients have before now occupied beds, been treated with expensive hormone preparations quite unnecessarily, and afterwards subjected to an irksome regime, when a complete cure could have been effected by simple avulsion of the little polyp.

TYPES OF ABORTION

The types of abortion commonly seen are set out in the following table —

TYPE	FEATURES	
Threatened	Slight pain, slight hæmorrhage, os closed or very slightly dilated Pregnancy may continue or abortion become inevitable	
Inevitable		
(a) Static	Presents as threatened abortion, but bleeding <i>persistent</i>	Pain slight or absent
(b) Dynamic	Expulsive state	Rhythmic painful contractions
Complete	Uterus empty Pain and hæmorrhage cease	
Incomplete		
(a) Recent	Some conceptional products remain in the uterus Hæmorrhage, which may be great, and/or pain continue	
(b) Remote	Ambulatory May simulate menorrhagia or functional uterine hæmorrhage	
Missed		
Intra-uterine death	(a) <i>Before</i> placenta formed	Result—blood or carneous mole Macerated or mummified fœtus and placenta passed
	(b) <i>After</i> placenta formed	

DIFFERENTIAL DIAGNOSIS

Threatened abortion—Attention has already been drawn to the importance of the mucous polyp. Erosion of the cervix in pregnancy may cause slight bleeding. When a speculum is passed the bright red appearance of erosion is typical, and if the cervix is wiped with cotton-wool there may be a little bleeding from the surface of the erosion, but no blood is seen issuing from the cervical canal, as in threatened abortion.

To distinguish threatened abortion from inevitable abortion on the one hand, and from incomplete abortion on the other, may be difficult. Perhaps only the passage of time will solve the problem.

Inevitable abortion—This means that the abortion is bound to happen in spite of any treatment that may be given. There appear to be two phases of inevitable abortion, the static and the dynamic, and in each a different picture is presented. The first, or static, is more liable to be mistaken for threatened abortion. In this the abortion sets in with bleeding; in quantity, at first, it suggests threatened abortion, but the bleeding goes on and on. When it has persisted for more than two to three weeks, abortion, in my experience, is sure to happen. The same conclusion would be reached in a shorter time when a greater amount of blood loss occurs. Sooner or later static inevitable abortion becomes dynamic. the uterus is starting to expel the ovum. Now the rhythmical, painful uterine contractions occur, with the dilating cervix and perhaps increased hæmorrhage, and soon the abortion is either complete or incomplete.

Incomplete abortion can also be regarded as having two phases presenting different pictures, the recent and the remote. The former, as the name suggests, is merely a dynamic inevitable abortion in which the uterus has failed to empty itself com-

pletely Here there may still be considerable hæmorrhage, continuing with or without intermittent labour-like pains This is the type of incomplete abortion which is so frequently sent into hospital as an emergency, the treatment of which will be discussed later It is not a matter of great moment in the first instance to distinguish this form of incomplete abortion from dynamic inevitable abortion with considerable hæmorrhage, for the initial treatment is the same In the remote incomplete abortion there may be a history of miscarriage having taken place some weeks previously, and of bleeding restarting and continuing after temporarily having ceased On the other hand, there may not be a definite history of the passage of an ovum, but only of continuous bleeding after a short period of amenorrhœa There need not even be any amenorrhœa Such a patient may arrive at an out-patient clinic looking quite well Pelvic examination reveals a normal or slightly enlarged uterus With a reliable history that an ovum has been passed the diagnosis is clear When, however, that is lacking, *functional uterine hæmorrhage* is a distinct possibility

Ectopic pregnancy—This important condition should not be overlooked, not the ruptured ectopic pregnancy, but one which is beginning to be disturbed Careful questioning may elicit a history of colicky abdominal pain with, perhaps a feeling of faintness, it may transpire that the bleeding has been slight and more in the form of a brown discharge than of frank blood Many signs have been described, but, with such a history, tenderness on manipulation of the cervix during vaginal examination would be extremely suggestive of ectopic pregnancy If the uterus were then found to be empty on curettage, laparotomy would be indicated so likely is the diagnosis to be correct So impressed have I been with the possibility of overlooking an extra-uterine pregnancy that I make it a rule to ask myself in any doubtful threatened or incomplete abortion, "Could this possibly be an ectopic pregnancy?" It is a safeguard against mistakes

Twice I have seen *carcinoma corporis uteri* simulate the remote type of incomplete abortion (Purdie, 1944)

Hydatidiform (vesicular) mole and *missed abortion* deserve consideration More commonly, patients with hydatid mole present themselves because of bleeding At first it is thought that the patient has a threatened abortion, or what I have called a static inevitable abortion When the bleeding is persistent, and the uterus larger than it ought to be by dates (the uterus is commonly, although not necessarily, larger than expected in this condition), hydatid mole should be considered seriously X-ray of the abdomen will show absence of fetal parts and the Aschheim-Zondek test is strongly positive In some cases lutein cysts of the ovary are distinctly palpable on vaginal examination These, in the presence of the foregoing history and uterine findings, make the diagnosis almost certain

Missed abortion—Here symptoms of threatened abortion occur and subside but the fetus dies, yet the whole ovum is retained in the uterus for weeks or even months If this intra-uterine death occurs before the formation of the placenta the uterine contents, when passed eventually, will be either a blood mole or a carneous mole, depending upon the length of time between intra-uterine death and expulsion, but if it occurs after the formation of the placenta, the fetus and placenta when passed will show either mummification or maceration The patient

may be the first to draw attention to the condition. She realizes that the uterus has stopped growing, notices the cessation of fetal movements, if quickening has already occurred, and appreciates retrogressive changes in the breasts. She may present herself for examination because of these signs, but quite commonly on account of a brown, or even black, discharge.

TREATMENT

THREATENED ABORTION—Etiology is discussed later, but two causes can conveniently be discussed here. These are (a) hypertension and (b) retroversion of the gravid uterus.

(a) *Hypertension*—The importance of blood pressure readings later in pregnancy is generally recognized, but routine estimation of the blood pressure in every case of abortion is also of value. Severe hypertension is a recognized cause of abortion. Abortion, so caused, particularly in the first trimester, may be a blessing in disguise, safeguarding the woman from later serious and perhaps fatal complications, such as eclampsia, accidental hæmorrhage, and symmetrical cortical necrosis of the kidneys.

If the taking of the blood pressure is neglected, then an attempt may be made by intensive treatment to prevent abortion occurring, when really it should be welcomed, or the patient may be given bad advice by encouraging her to try again when, perhaps, pregnancy ought to be discouraged or sterilization recommended.

(b) *Retroversion of the gravid uterus* may be found. If the position of the uterus can be corrected easily and gently into one of anteversion this should be done and a Hodge type of pessary inserted. This is left in position until after the twelfth week, when the retroversion will not recur following its removal. If the slightest difficulty is experienced in replacing the uterus when the patient is seen for the first time, it should be left untouched. The next day it may be possible to replace it with the care and gentleness necessary if the pregnancy is not to be disturbed. Should this not be possible, a well-fitting rubber ring pessary may be inserted while the uterus is still retroverted, and the patient encouraged to lie on her face. In many cases the uterus will then correct itself. (It will be realized that this applies only to the retroverted gravid uterus.)

When the patient has a retroverted uterus the practitioner may be called in, not because of threatened abortion but because of retention of urine with overflow. This occurs usually between the twelfth and fourteenth weeks. In most cases the remedy is simple. A catheter is tied in *per urethram* and the bladder decompressed slowly (the method of using the dripper of an intravenous saline apparatus described by Hamilton Bailey is excellent) until in twenty-four to thirty-six hours it is empty, when it will be found that the uterus has corrected itself. The uterus will not fall back into retroversion, it is too big to do so. This simple method of replacement is most effective. The alternative of emptying the bladder at once by catheter and attempting manipulative correction of the incarcerated uterus is more likely than not to fail (perhaps even under anaesthesia), whilst the force necessary for success may be sufficient to make abortion inevitable.

However divergent the views held as to the efficacy of the different remedies used in the treatment of threatened abortion, there is agreement on rest in bed. The patient should go to bed at once and remain there (without bathroom privileges) for at least a week after all bleeding has stopped. Morphine, $\frac{1}{2}$ grain or even $\frac{1}{2}$ grain immediately, followed by $\frac{1}{2}$ grain four- or six-hourly for the next twenty-

four hours, is time-honoured and widely used at present. There is evidence (Greenhill, 1943), however, that in early pregnancy, morphine and the other opium alkaloids increase uterine tone and stimulate uterine contraction. Objection can therefore be raised to the giving of morphine and a case made out for the use of barbiturates, or other mild sedatives. Progesterone is frequently given, either empirically or after estimation of the urinary pregnandiol, when, if that is low, deficiency of corpus luteum hormone is postulated. There is no uniformly accepted dosage. Injections of progesterone, 5 to 10 mgm, twice daily at first, gradually cut down to once every second or third day while the patient is in bed, followed by weekly injections until about the sixteenth week, are commonly given. Successful results are claimed. On the other hand, even when the weekly dosage of progesterone (administered daily or every other day) was higher than usual, even reaching 140 mgm (Hamblen, 1942) the results have proved disappointing. In fact it has been suggested that progesterone may cause pain, if not actual uterine contractions (Kurzrok *et al*, 1937, Bickers, 1942). Stilbæstrol in large doses has been advocated by Karnaky (1942) for the treatment of threatened abortion and good results are claimed, whereas he has had poor results with progesterone. Theoretically, stilbæstrol should increase uterine contraction and its use in threatened abortion appears to be quite irrational. There are conflicting opinions about the value of vitamin E therapy. The anti-hæmorrhagic vitamins C and I (Javert and Stander, 1943) are said to have been used with success. From these divergent claims it is evident that there is as yet no satisfactory single remedy or combination of remedies. It is obvious that in many cases foetal death or deformity on the one hand, or gross abnormality of implantation or of the decidua on the other, may be present before any treatment is started. Abortion then occurs in spite of treatment. The evaluation of any remedy is likely to remain difficult.

INEVITABLE ABORTION—(a) *Static inevitable abortion*—Here, the picture is that of a persistent and prolonged threatening of abortion. Neither on clinical nor on biochemical grounds is it possible to say with certainty that the patient is going to abort. Therefore expectant treatment of whatever kind the practitioner favours should be continued, unless the persistent loss of blood is such that the patient is becoming progressively anæmic. By that time the uterus is usually too large to allow of dilatation of the cervix and evacuation of uterus *per vaginam* with safety at one sitting. Repeated manipulations, such as the insertion of laminaria tents, followed twenty-four hours later by wide dilatation of the cervix and uterine evacuation, are liable to be followed by sepsis. It is better to encourage the uterus to empty itself by giving the patient some form of drug induction.

One useful scheme is to give large doses of stilbæstrol orally, e.g., 25 mgm at hourly intervals for six or eight doses, to render the uterus more sensitive to the oxytocic drugs followed by castor oil 1 ounce (preferably on an empty stomach), a hot bath and an enema and then intramuscular injections of 2.5 obstetric units of pituitrin at hourly intervals for six doses. The whole may be repeated on a second occasion a day or two later.

With this drug induction the patient may pass from the static to the dynamic phase of inevitable abortion, and soon the whole process may be complete. Some do not proceed to the dynamic phase and the bleeding stops, the whole process settles down and the pregnancy continues, either for the time being only to abort later, but quite often to factual viability. It is well known that drugs will seldom

produce abortion of a normal pregnancy Having made the diagnosis of static inevitable abortion *when bleeding is persistent in spite of rest in bed and sedatives*, it is my practice to give the patient a drug induction and to regard it as a therapeutic test of "inevitability" If abortion is really inevitable it will pass into the dynamic phase. If it is not it will not do so, and no harm has been done, whilst if the bleeding stops completely the result is satisfactory

(b) *Dynamic inevitable abortion* — This may proceed uneventfully as a miniature labour When complete, an oxytocic drug is given to prevent atonic hæmorrhage Whereas some inevitable abortions occur with little hæmorrhage, in others it is a marked feature, then there may be little difference in the clinical picture from that of the *recent incomplete abortion* with considerable hæmorrhage It is convenient to consider these together

The guiding principles of treatment are (i) to arrest the hæmorrhage and prevent its recurrence, (ii) to stimulate the uterus to expel its contents or, if it is unable to do so, to empty it of its contents, and (iii) to treat for shock and blood loss The patient is usually first seen in her own home where she may be looked after, but often she is sent to a hospital or nursing home after preliminary treatment Consider the ill patient who is usually transferred —

The practitioner arrives to find her steadily losing blood Perhaps she has been doing so for several hours She is pale, but the pulse rate is not much raised, although a lot of blood and clots are present in the bed To leave her in that state and arrange for her transfer to hospital with no active treatment, even if she has apparently stopped losing, is a mistake She may be much worse when she arrives there

Shenkin *et al* (1944) bled healthy volunteers of large quantities of blood. They found that the recumbent subject could be bled "to the point of collapse without exhibiting conspicuous tachycardia, diminished blood pressure or other noteworthy abnormalities" If the subject then sat up he fainted Apply this to our patient.

The practitioner left her "not too bad" She goes on bleeding quietly while waiting for the ambulance As she is being lifted on to a stretcher or carried down narrow stairs she sits up, or is put in an almost upright position She is suddenly overwhelmed and collapses, and arrives in hospital deathly pale, cold, with an extremely low blood pressure and almost non-existent pulse. She will now require transfusion of blood or plasma, which might have been avoided—and it should be remembered that deaths do occur attributable directly to transfusion. First she should be given ergometrine*, 0.5 mgm intramuscularly Then such blood clot as is present in the vagina should be scooped out gently, with any placental tissue which happens to be lying there This makes the patient more comfortable, and with these two measures the hæmorrhage will probably cease At this stage a finger should not be inserted into the uterus in an attempt to remove placental tissue That is likely to produce further bleeding

Objection is sometimes raised to the removal of blood clot from the vagina because of lack of aseptic and antiseptic facilities in unsuitable surroundings This can largely be overcome by wearing clean (not sterile) rubber gloves on socially clean hands and rubbing the equivalent of a level teaspoonful of 30 per cent dettol cream on to the gloves for two minutes with the motions of hand washing (Colebrook, 1933) Dettol cream can also be used on the vulva Ergometrine given intramuscularly takes four minutes to act The practitioner can therefore assure himself that bleeding has stopped before he leaves the patient. Some

* The most effective oxytocic is alkaloid of ergot. Acts in 3 to 4 minutes when given intramuscularly Action lasts upwards of an hour Known as ergonovine in American literature

practitioners like to give morphine. It is of value in combating shock, it may allay the patient's mental anxiety, but, given alone without any oxytocic drug, it is useless in the arrest of hæmorrhage. Far better omit the morphine than the ergometrine, and in septic abortions (see p. 43) in which peritonitis may be present, it is much better not to give it. I would strongly recommend practitioners who send abort patients into hospital to give 0.5 mgm of ergometrine intramuscularly before leaving the patient's house, even if they do not remove the vaginal blood clots either from reluctance to do so or personal disapproval of the practice. By this simple single measure, one intramuscular injection, many a transfusion would be avoided and many a convalescence shortened.

On arrival in hospital what then? The principles enunciated are put into action. Ergometrine, 0.5 mgm, is given intramuscularly, with or without morphine, $\frac{1}{4}$ grain, and the ergometrine alone is repeated in one hour, two hours and then four hours until the uterus is evacuated under general anaesthesia. If a considerable interval must elapse before this is done the ergometrine is not given for more than two hours, unless necessitated by hæmorrhage. The patient must be fit for anaesthesia before attempting evacuation. With the firm uterine contractions induced by these measures the bleeding will stop, particularly if the vagina is gently cleared of clots and of any placental tissue which, protruding through the cervix, is *more in the vagina than the uterus*, but if this tissue is protruding to such a small extent that more of it is in the uterus than in the vagina it should *not* be dislodged at this juncture, for the attempt will probably fail, and only result in further bleeding and increase of shock. Most patients recover quickly with this treatment and soon are fairly fit, although the uterus still contains some products of conception. Now a soap and water enema is given. This empties the often loaded rectum and allows of accurate pelvic findings later, whilst quite large portions of placental tissue may be expelled when the enema is being returned. This is an advantage for the smaller the amount of tissue which has to be removed finally from the uterus the less blood the patient is likely to lose at operation.

The few who do not respond, and those who are exsanguinated on admission, require, in addition, a transfusion of blood or a blood substitute. Ideally the blood should be compatible blood of the same blood group as the patient's. It should be from an Rh-negative donor. This is not yet universally practicable. If blood of unknown Rh factor has to be given, the patient's past child-bearing history should be considered carefully. Such blood should not be given if the history suggests that she may have become immunized to the Rh factor (e.g. erythroblastosis, jaundice of the new born, unexplained still-birth, repeated miscarriages, previous blood transfusion). Thus bleeding is stopped and prevented from recurring, whilst blood loss is treated by replacement.

There is no comparison possible between the management of severe hæmorrhage in incomplete abortion and ruptured ectopic pregnancy with a belly full of blood. In the latter the only means of arresting the hæmorrhage is immediate laparotomy. No matter how desperate the case may be, it is futile to attempt to make the patient fit first, and the bleeding is stopped by placing a clamp across the bleeding vessels. But in abortion the clamp is the contractile power of the uterus and the hand that closes the clamp is the oxytocic drug.

It is unnecessary to describe in detail the operation of *evacuation of the uterus*, but for the benefit of those who may be called upon occasionally to perform it some points are worth considering. The pelvic findings should be confirmed under anaesthesia before any operation.

step is taken. This is important, for a previously anteverted uterus may have fallen back with the adoption of the lithotomy position and, unless this is known, the first instrument inserted into the uterus may perforate its anterior wall. Moreover, the opportunity for the detection of any other pelvic abnormality should not be missed. This necessitates a temporarily deep anaesthesia which is undesirable in the later stages, since it predisposes to atonic hæmorrhage. The ideal anaesthetic therefore requires an anaesthetist of considerable skill. All manipulations should be gentle because of the possibility of perforating the uterus. Also the more gentle the handling the less likely is morbidity afterwards. For this reason I have referred to the operation as evacuation of the uterus, not curettage. I do not agree with curetting the uterine wall in a recent abortion. Hæmorrhage sometimes occurs during the operation or when it is thought to have been completed. It may be troublesome and sometimes even alarming. In order to deal with this effectively the cause must be understood. It is due to one or more of the following—(a) retained products which have been overlooked, (b) atony of the uterus, or (c) trauma, these should be reviewed systematically. A finger is inserted into the uterus—the little finger may go in when the index finger will not—and the uterus is pushed down upon the examining finger by the left hand upon the patient's abdomen. If there is any tissue inside it should be removed. If the bleeding does not stop now, the uterus should be "rubbed up" between the abdominal hand and the fingers in the vagina. If it remains soft, ergometrine 0.5 mgm or pituitrin 0.25 c.cm. (2.5 units) can be given intravenously, perhaps by the anaesthetist. Failing that, if the hæmorrhage is too sharp to be treated by intramuscular injection, it can be given through the abdominal wall into the uterine muscle, which is almost as effective as the intravenous route itself. Certain conditions, not always emphasized as they ought to be, which *must* be fulfilled to make this practice safe (Mour, 1944) are that the bladder should be empty, the uterus should be manipulated into contact with the abdominal wall at the site of the proposed injection, and the abdominal skin should be sterilized, whilst the syringe and needle (which should be of stainless steel to lessen the risk of its snapping) should be sterilized by boiling.

Prevention of atonic hæmorrhage is better still. This is often achieved by the injection of ergometrine, 0.5 mgm intramuscularly, as soon as the patient is anaesthetized, *before* the pre-operative local cleansing is begun. Alternatively, in those patients who are having intravenous anaesthesia, it may be given with the anaesthetic drug. If the bleeding continues after eliminating the first two causes it must be due to trauma. The cervix may have been split during dilatation and one or more catgut sutures may prove necessary if bleeding is smart. Again, prevention is better. When cervical dilatation is required do not over-dilate, for even if the cervix does not split externally it may do so internally between the external and internal os. This can be detected by inserting the little finger and feeling the walls of the cervical canal. If these measures for the prevention and control of bleeding are followed, the undesirable practice of packing the uterus will almost never be required.

Provided that the patient feels well, and her temperature remains afebrile, and there is no gross anæmia, she is allowed up forty-eight hours later and can go home the next day. The practitioner should look for anæmia in these patients, and if it is present they should receive adequate iron therapy, with hæmoglobin estimations from time to time to ensure that there is a good response to treatment. This necessitates enthusiasm with tactful doggedness on the practitioner's part, for many of these patients, with their numerous domestic cares, become accustomed to a considerable degree of anæmia and scorn the necessity for treatment. Too often they become pregnant again while still anæmic.

SEPTIC ABORTION

Sepsis may develop while the patient is under treatment or before she seeks medical advice or admission to hospital. The common case is that of an incomplete abortion with some pyrexia, the uterine contents are somewhat offensive but there are no abnormal abdominal signs. My own practice is to evacuate the uterus with great gentleness, and in the majority of cases convalescence is surprisingly smooth. Should the uterine contents be frankly offensive, intra-uterine glycerin (Hobbs,

1927) is given. Should there be any toxic appearance, a sulphonamide is given until the result of high vaginal swab culture is known, when the drug can be continued if indicated.

There are conflicting views on the wisdom of evacuating the uterus if there is any sepsis present, as judged by the presence of pyrexia. Some maintain that expectant treatment should be adopted in every case with pyrexia, and quote figures to show that in any large series treated actively, mortality and morbidity are approximately double that resulting from expectant treatment. Others, considering that it is a well-founded surgical principle to remove a removable focus of infection, defy the conservative school and point to the well-recognized cases of local pelvic and general extensions of infection which do occur under conservative treatment, and attribute these to the delay involved. Both are agreed that, in the presence of established local pelvic spread of infection (e.g., when an extra-uterine mass is palpable), active measures are definitely contraindicated.

When widely divergent views are held by honest thoughtful men over some difficult matter the usual explanation is that the whole truth lies with neither. Rutherford (1943) takes a cervical smear in these cases and treats them conservatively for twenty-four hours while awaiting the bacteriological report. During this time he gives sulfadiazine. If the culture shows no predominance of hæmolytic streptococci, and if there is no parametrial involvement, he cures the uterus even in the presence of fever or of a history of previous instrumentation. If there is a predominance of hæmolytic streptococci, sulfadiazine and expectant treatment are continued and the uterus is not curetted until the patient has been afebrile for three days. This seems a reasonable method of approach (although I should recommend evacuation of the uterus rather than curettage) and is one not committed wholly to either school. Studdiford (1939) followed a somewhat similar routine in 1,248 cases from 1934 to 1937, but did not use sulphonamides. His mortality was 1.2 per cent, whilst the average post-operative stay in hospital was 2.9 days. In a control series (1920 to 1933) of 7,184 cases treated conservatively the mortality was 1.48 per cent. The difference is not statistically significant. Certain it is that purely conservative treatment means much longer hospitalization than is the case with some more active measures. Browne (1944) is a staunch supporter of conservative treatment, but quotes no evidence later than 1923 in support of his argument.

General peritonitis may be present with incomplete abortion, even in the absence of any perforation of the vagina or uterus. Its diagnosis presents difficulties similar to the diagnosis of puerperal peritonitis following child-birth. In the latter it is quite common, at any rate in hæmolytic streptococcal cases, not to operate for peritonitis but to rely solely on chemotherapy. That may be reasonable. The clinician, experienced in puerperal fever, can frequently diagnose hæmolytic streptococcal infection with fair accuracy on clinical grounds alone. In my experience, however, post-abortion peritonitis is more frequently due to other organisms, e.g. coliform bacilli, staphylococci or non-hæmolytic streptococci, in which (for peritonitis) the sulphonamide drugs are useless. I therefore open the abdomen with a small incision, and insert a corrugated rubber drain down to the pouch of Douglas, and give chemotherapy in addition only if the bacteriology of the

nal tract or peritoneum calls for it. Although I have had occasion to regret failure to drain I have yet to regret having done so. The uterus is usually evacuated before the laparotomy.

An interesting, but infrequent problem is the patient who has a static inevitable abortion with general peritonitis, without any perforation, whilst the uterus is too large to allow of evacuation from below, even if that were desirable. This has been met by the insertion of a corrugated abdominal drain. The patient's condition has improved and abortion has taken place spontaneously some days later.

It is not wise to treat a septic, and possibly criminal, abortion at home without a second opinion, for the practitioner may bring suspicion of complicity upon himself.

A practitioner sent a woman, whom he had been attending at home for some days, into hospital where I was house-surgeon. He had treated her with intra-uterine glycerin foam calling in a consultant. In hospital, only laparotomy with drainage was performed. She died, and at autopsy a perforation about half an inch in diameter was found in the uterus. An abortionist had done it, but that practitioner, whose innocence I never doubted, it was very uncomfortable until the inquest was over.

Pyrexia following miscarriage is notifiable as puerperal pyrexia. Its investigation could be similar, and the importance of cervical or high vaginal swab culture (aerobic and anaerobic) should not be forgotten. Until now anaerobic streptococcal infection has defied all specific measures. Cruickshank (1944) has found a number of strains penicillin-sensitive. Although clinical trial has been disappointing his results do not contraindicate further trial.

OTHER TYPES

EMOTE INCOMPLETE ABORTION—Curettage is the best treatment and the sharp curette should be used. It is well to be gentle, for the uterine wall may still be soft and perforation is easier than with the normal uterus.

ABORTION IN THE LATER WEEKS—The nearer to the twenty-eighth week of pregnancy the more its features are those of labour, and the less desirable is it to explore the uterus—uncontrollable hæmorrhage is the only indication. The breasts may become engorged. Relief is readily obtained by giving an œstrogen (stilbæstrol, 5 mgm. four-hourly for three days and eight-hourly for another three days, from the onset of symptoms, is adequate. It is quite unnecessary to purge, and the breasts or restrict fluids.

HYDATIDIFORM MOLE—If the patient is aborting when seen, provided that bleeding is not excessive, the uterus should be encouraged to empty itself by the administration of oxytocic drugs, after which any remaining portions are easily and safely evacuated. But care must be taken to ensure that the uterus is well contracted while doing so, for hæmorrhage will then be less, and the very real danger of perforation rendered less likely. If the patient is not aborting, and cannot be induced with drug induction to abort, the uterus should be evacuated. With a small uterus, cervical dilatation (in some cases using laminaria tents for twelve hours previously) and evacuation of the uterus *per vaginam* may be performed. Preparations should be made beforehand for blood transfusion in case it is required, and 3-inch wide gauze packing should be available, although every effort should be made to render its use unnecessary. When the uterus is larger (more than fourteen to sixteen weeks' size) I have a strong preference for abdominal hysterotomy. Objection is sometimes made on the grounds of possible contamination of the abdominal wound and contents with split vesicles, sepsis with peritonitis is also a danger because

1927) is given. Should there be any toxic appearance, a sulphonamide is given until the result of high vaginal swab culture is known, when the drug can be continued if indicated.

There are conflicting views on the wisdom of evacuating the uterus if there is any sepsis present, as judged by the presence of pyrexia. Some maintain that expectant treatment should be adopted in every case with pyrexia, and quote figures to show that in any large series treated actively, mortality and morbidity are approximately double that resulting from expectant treatment. Others, considering that it is a well-founded surgical principle to remove a removable focus of infection, defy the conservative school and point to the well-recognized cases of local pelvic and general extensions of infection which do occur under conservative treatment, and attribute these to the delay involved. Both are agreed that, in the presence of established local pelvic spread of infection (e.g., when an extra-uterine mass is palpable), active measures are definitely contraindicated.

When widely divergent views are held by honest thoughtful men over some difficult matter the usual explanation is that the whole truth lies with neither. Rutherford (1943) takes a cervical smear in these cases and treats them conservatively for twenty-four hours while awaiting the bacteriological report. During this time he gives sulfadiazine. If the culture shows no predominance of hæmolytic streptococci, and if there is no parametrial involvement, he cures the uterus even in the presence of fever or of a history of previous instrumentation. If there is a predominance of hæmolytic streptococci, sulfadiazine and expectant treatment are continued and the uterus is not curetted until the patient has been afebrile for three days. This seems a reasonable method of approach (although I should recommend evacuation of the uterus rather than curettage) and is one not committed wholly to either school. Studdiford (1939) followed a somewhat similar routine in 1,248 cases from 1934 to 1937, but did not use sulphonamides. His mortality was 1.2 per cent, whilst the average post-operative stay in hospital was 2.9 days. In a control series (1920 to 1933) of 7,184 cases treated conservatively, the mortality was 1.48 per cent. The difference is not statistically significant. Certain it is that purely conservative treatment means much longer hospitalization than is the case with some more active measures. Browne (1944) is a staunch supporter of conservative treatment, but quotes no evidence later than 1923 in support of his argument.

General peritonitis may be present with incomplete abortion, even in the absence of any perforation of the vagina or uterus. Its diagnosis presents difficulties similar to the diagnosis of puerperal peritonitis following child-birth. In the latter it is quite common, at any rate in hæmolytic streptococcal cases, not to operate for peritonitis but to rely solely on chemotherapy. That may be reasonable. The clinician, experienced in puerperal fever, can frequently diagnose hæmolytic streptococcal infection with fair accuracy on clinical grounds alone. In my experience, however, post-abortion peritonitis is more frequently due to other organisms, e.g., coliform bacilli, staphylococci or non-hæmolytic streptococci, in which (for peritonitis) the sulphonamide drugs are useless. I therefore open the abdomen with a small incision, and insert a corrugated rubber drain down to the pouch of Douglas, and give chemotherapy in addition only if the bacteriology of the

tal tract or peritoneum calls for it. Although I have had occasion to regret re to drain I have yet to regret having done so. The uterus is usually evacuated re the laparotomy.

interesting, but infrequent problem is the patient who has a static inevitable abortion: general peritonitis, without any perforation, whilst the uterus is too large to allow of evacuation from below, even if that were desirable. This has been met by the insertion corrugated abdominal drain. The patient's condition has improved and abortion has place spontaneously some days later.

is not wise to treat a septic, and possibly criminal, abortion at home without a second ion, for the practitioner may bring suspicion of complicity upon himself.

practitioner sent a woman, whom he had been attending at home for some days, into spital where I was house-surgeon. He had treated her with intra-uterine glycerin e calling in a consultant. In hospital, only laparotomy with drainage was performed died, and at autopsy a perforation about half an inch in diameter was found in the is. An abortionist had done it, but that practitioner, whose innocence I never doubted, very uncomfortable until the inquest was over.

pyrexia following miscarriage is notifiable as puerperal pyrexia. Its investigation ould be similar, and the importance of cervical or high vaginal swab culture (obic and anaerobic) should not be forgotten. Until now anaerobic streptococcal ction has defied all specific measures. Cruickshank (1944) has found a number strains penicillin-sensitive. Although clinical trial has been disappointing his ilitis do not contraindicate further trial.

OTHER TYPES

NOTE INCOMPLETE ABORTION—Curettage is the best treatment and the rp curette should be used. It is well to be gentle, for the uterine wall may still soft and perforation is easier than with the normal uterus.

ABORTION IN THE LATER WEEKS—The nearer to the twenty-eighth week pregnancy the more its features are those of labour, and the less desirable is it explore the uterus—uncontrollable hæmorrhage is the only indication. The asts may become engorged. Relief is readily obtained by giving an œstrogen lbœstrol, 5 mgm four-hourly for three days and eight-hourly for another three s, from the onset of symptoms, is adequate. It is quite unnecessary to purge, d the breasts or restrict fluids.

HYDATIDIFORM MOLE—If the patient is aborting when seen, provided that eding is not excessive, the uterus should be encouraged to empty itself by the ministration of oxytocic drugs, after which any remaining portions are easily and ely evacuated. But care must be taken to ensure that the uterus is well contracted ible doing so, for hæmorrhage will then be less, and the very real danger of perfora- n rendered less likely. If the patient is not aborting, and cannot be induced with ug induction to abort, the uterus should be evacuated. With a small uterus, vical dilatation (in some cases using laminaria tents for twelve hours previously) d evacuation of the uterus *per vaginam* may be performed. Preparations should e made beforehand for blood transfusion in case it is required, and 3-inch wide uze packing should be available, although every effort should be made to render use unnecessary. When the uterus is larger (more than fourteen to sixteen ecks' size) I have a strong preference for abdominal hysterotomy. Objection is metimes made on the grounds of possible contamination of the abdominal wound id contents with spilt vesicles, sepsis with peritonitis is also a danger because

blood clot, an excellent culture medium, may have formed in the lower part of the uterus if the patient has been bleeding for any time, moreover, the protection afforded by amnion and normal chorion are missing. On the other hand, evacuation *per vaginam* may result in such severe hæmorrhage that the uterus and vaginæ require to be packed. I have known the operation to be abandoned when the uterus had only been half emptied, and packing introduced because of alarming hæmorrhage. The uterus had still to be evacuated later on. In such circumstance it is not surprising that sepsis followed. Compare this with a clean abdominal operation, in which the uterus, injected with pituitrin, contracts and visibly blanches before it is incised, when the mole can be squeezed out of the uterine incision, leaving an almost bloodless field. The repair is simple. Precautions can be taken against the spilling of vesicles. My experience of abdominal hysterotomy has convinced me that its advantages outweigh its reputed disadvantages.

MISSED ABORTION—In most cases the uterus will empty itself in time. Stilbæstrol-pituitrin induction, perhaps repeated, has a high measure of success. Bleeding is usually slight. It is occasionally necessary to evacuate the uterus and this is generally easy to do, for the fœtus is soft and easily crushed.

Sometimes a patient claims maternity benefit because of a missed abortion. In certain circumstances, which a concrete example will explain, she may do so successfully.

A woman becomes pregnant and the fœtus dies in utero at the twelfth week, but the ovum is retained until the thirtieth week, when it is passed as a missed abortion. Provided that she would be entitled to benefit for a live or still-birth she would be entitled to it for this missed abortion (Controller, Ministry of Health, 1944). She is eligible for benefit because the products of conception have been in the maternal body for more than twenty-eight weeks. The usual Maternity Benefit claim form is filled in with the appropriate certificate by the medical practitioner or midwife. In the example cited the sex of the child, for practical purposes, could not be told. It is in order to delete from any such printed certificate the words relating to sex and to furnish with it a brief statement of the circumstance (Controller, M o H, 1944). It is really regarded as a unique type of still-birth. As such, however, the "birth" would require to be notified, registered and a still-birth certificate issued (Registrar-General, 1945). Disposal would be by burial or cremation.

This seems rather an absurd procedure over an object which is in fact an abortion and could well be disposed of like any other abortion, but for the patient's claim. It might cost her £1 to bury it, but if she had a right to double benefit she might consider the net gain of £3 worth the trouble involved.

ETIOLOGY

The patient wants to know why the abortion occurred and if it will happen again. A comprehensive list of causes can be found in most textbooks. Any likely cause of recurrence, such as a submucous uterine fibroid, should be dealt with before another pregnancy is attempted, but less likely causes, such as uterine retroversion, should not be treated surgically unless the patient is an *habitual aborter*. The more completely such a case is investigated the less is the chance of overlooking a possible demonstrable cause. The importance of hypertension has been stressed. Statements that syphilis has been over-blamed as a cause of abortion should not deter from determining the Wassermann reaction of the blood—especially in late abortion. The Rh factor should be ascertained, if the patient is Rh-negative with Rh-positive antibodies and the husband is Rh-positive, there is at present nothing that can be

done about it, unless to advise birth control. Of the less obvious pelvic lesions severe cervical lacerations call for treatment. Particularly distressing is the case in which too high an amputation of the cervix has previously been performed, there is no treatment apart from rest in bed—and that may fail. Early developmental errors are often overlooked. In recurrent abortion "*cherchez le mari*" should not be forgotten.

HABITUAL ABORTION

No woman should be regarded as an habitual aborter until she has had at least three consecutive abortions of spontaneous onset. The element of chance is otherwise too great. All possible causes should be eliminated so far as possible. When the next pregnancy has begun, adequate diet (Toronto, and People's League of Health experiments) is of great importance. Rest and sleep are essential. Coitus should be banned. It is often advised that patients should rest in bed at the time of the suppressed periods—harmless advice, but how often, I wonder, do the days of rest and those of the suppressed periods coincide? Which of the various fashionable hormone or vitamin preparations should be given? It seems fairly well established now in practice that, in addition to general advice along the lines indicated, progesterone, 5 to 10 mgm, is given weekly until about the twenty-sixth week. Vitamin E may also be given daily throughout the whole pregnancy, either alone or in addition to the progesterone therapy. It should be understood quite clearly, however, that there is not yet a sufficient number of large *well-controlled* series of cases published to justify the assumption that these alleged preventive measures are all that some enthusiasts claim. Thyroid extract in small daily doses is also advocated. No matter what treatment is given there will be apparent successes. The whole position of these so-called remedies is still *sub judice*. When all measures have failed in a woman who is really desperate to bear a child the possibility of rest in bed, if necessary for the entire pregnancy, should be considered. Attention would then have to be paid to diet, regulation of the bowels, massage and suitable exercises to keep up muscular tone. Success has followed this in the past.

References

- Bailey, H. (1944) "Pye's Surgical Handicraft," 14th edition, Bristol, 173.
 Bickers, W. (1942) *Amer J Obst Gynec*, 43, 663.
 Browne, F. J. (1944) "Antenatal and Postnatal Care," 5th edition, London, 182.
 Colebrook, L. (1933) *J Obst Gynec Brit Emp*, 40, 981.
 Cruickshank, R. (1944) *Proc. roy Soc Med*, 37, 506.
 Ebbs, J. H., Tisdall, F. F., and Scott, W. A. (1941) *J Nutrit*, 22, 515.
 Greenhill, J. P. (1943) *Year Book Obst Gynec*, 49 (Editorial comment).
 Hamblen, E. C. (1942) *Texas State J Med*, 38, 488.
 Hobbs, J. R. (1927) *Brit med J*, 2, 1223.
 Interim Report of the People's League of Health (1942) *Lancet*, 2, 10.
 Javert, C. T., and Stander, H. J. (1943) *Surg Gynec Obst*, 76, 115.
 Karnaky, K. J. (1942) *South med J*, 35, 838.
 Kurzrok, R., et al. (1937) *Endocrinology*, 21, 341.
 Ministry of Health, Controller Insurance Dept. (1944) Personal Communication.
 Moir, J. C. (1944) *Brit med J*, 2, 606.
 Purdie, A. W. (1944) *Proc roy Soc Med*, 37, 426.
 Registrar-General (1945) Personal Communication.
 Rutherford, R. N. (1943) *West J Surg*, 51, 257.
 Shenkin, H. A., et al. (1944) *Amer J med Sci*, 208, 421.
 Studdiford, W. E. (1939) *N Y St J Med*, 39, 1274.

CHILD HEALTH

XIII—VENEREAL DISEASE SERVICES

By M MICHAEL-SHAW, M B, B S

Director, Venereal Disease Department, Royal Free Hospital

THE VENEREAL DISEASES SERVICE

BEFORE considering the special problems arising in children, it is necessary to review the measures which have been taken to provide facilities for the control of venereal diseases in this country

The history of the Venereal Diseases Scheme dates from 1916, the year in which was published "The Final Report of the Royal Commission on Venereal Diseases". Before that date there had been an International Conference on Syphilis and Venereal Diseases held in Brussels, 1899, and a later conference in 1902. At the former there had been passed a resolution proposed by the British Medical Association "that all the Governments should appoint in each country a commission charged (a) to determine the frequency of venereal diseases in the civil population, (b) to enquire as to facilities for treatment already available, (c) to collect opinions as to the best means of controlling venereal diseases."

At the second conference among resolutions passed were two which should be mentioned —

- (1) That treatment of venereal diseases by unqualified people should be forbidden by law
- (2) That free and confidential treatment should be available

In this country men and women—medical and lay—had pressed for a Royal Commission to investigate the subject, but not until 1913 was such a commission appointed. The terms of appointment were "to enquire into the prevalence of venereal diseases in the United Kingdom, their effects upon the health of the community, and the means by which those effects can be alleviated or prevented."

The Final Report is divided into five sections, viz —

Section I which comprises an introduction summarizing previous state action and a section describing the venereal diseases and means of transmission

Section II Prevalence

Section III Effects

Section IV Means of alleviation or prevention

Section V Summary of recommendations and general conclusions

The report presents a detailed picture of conditions at the time, and provides for interesting comparison as regards venereal diseases during the two world wars. However, it is the practical recommendations which are of importance here.

From the total number of thirty-five recommendations the following were of primary importance —

- (1) "Measures should be taken to render the best modern treatment of venereal diseases readily available for the whole community and the arrangements should be such

that persons affected by these diseases will have no hesitation in taking advantage of the facilities for treatment which are afforded

- (2) The organisation of these means of treatment should be in the hands of the larger local authorities (the councils of counties and county boroughs) These authorities should, subject to the approval of the Local Government Board, organize and carry into effect definite schemes for dealing with the diseases
- (3) Institutional treatment should, as far as possible, be provided at general hospitals
- (4) Treatment at any institution, included in a local authority's scheme, should be free to all There should be no refusal to treat a patient who is unwilling to go to his own doctor
- (5) The treatment afforded at any institution should not be restricted to persons resident in a particular area.
- (6) Special arrangements, such as evening clinics, should be made for the treatment of out-patients at hours convenient to the working classes
- (7) Subject to proper safeguards, local authorities should be empowered to supply salvarsan or its substitutes gratuitously
- (8) The expenditure on schemes of treatment should be assisted by grants from Imperial Funds It is suggested that these grants should be equivalent to 75 per cent. of the expenditure incurred by local authorities The Local Government Board should be responsible for the distribution of these grants and should lay down the conditions subject to which the grants are to be paid
- (9) Extended facilities should be made available for the diagnosis of venereal diseases by laboratory methods

The organization of this service should be entrusted to the larger local authorities (county councils and county borough councils) and should form a part of the provision of laboratory facilities having for their object the prevention, diagnosis and treatment of diseases in general

In any schemes framed by local authorities the fullest use should be made of the laboratory facilities at Universities and Hospitals

The cost of this service should be met as to 75 per cent. from Imperial Funds and as to 25 per cent. from Local Rates "

These selected recommendations were to form the basis of the Venereal Diseases Scheme but there were, in addition, recommendations on the instruction of medical students in venereal diseases, on the implementing of the recommendations of the Select Committee on Patent Medicines, prohibiting all advertisements of remedies for venereal diseases, and on instruction for children, adolescents, and adults in matters relating to venereal diseases Prompt action was taken following the report, and in July 1916 were issued the regulations known as "The Public Health (Venereal Diseases) Regulations, 1916 " These were short and the first two articles outline the obligations laid on County Councils and County Borough Councils —

Article I—Every Council *shall*, subject to the approval of the Local Government Board, make arrangements for enabling any medical practitioner, practising in the area of the Council, to obtain, at the cost of the Council, a scientific report on any material which the medical practitioner may submit from a patient suspected to be suffering from venereal disease

Article II—(1) Every Council *shall* prepare and submit to the Local Government Board a scheme—

- (a) For the treatment at and in hospitals or other institutions of persons suffering from venereal disease, and
 - (b) For supplying medical practitioners with salvarsan or its substitutes for the treatment and prevention of venereal disease, and when the Board have approved the scheme the Council shall make arrangements for carrying it into effect at the cost of the Council
- (2) All information obtained in regard to any person treated under a scheme approved in pursuance of this Article shall be regarded as confidential.

Two articles of the regulation contained the word "may" instead of "shall", these concerned arrangements made with hospitals or institutions and the giving

of instructional lectures and publication of information on questions relating to venereal disease. In these regulations it is stated that "venereal disease" means syphilis, gonorrhœa and soft chancre.

Together with the regulations were issued —

- (a) A letter to Councils by the Secretary, Local Government Board, relating the findings of the Royal Commission and suggestions for methods to be adopted in carrying out the regulations
- (b) A letter to general and special hospitals asking for the "active cooperation" of such hospitals
- (c) A letter to Boards of Guardians asking that "Poor Law Medical Officers will make full use of these facilities," and a
- (d) "Memorandum by the Medical Officer of the Local Government Board on the Organization of Medical Measures." In this memorandum special references were made to the relation of the general practitioner to the official scheme as follows—
 - (i) "Every medical practitioner within a given administrative area, whether treating patients under the National Insurance Acts, or otherwise, should be informed by the medical officer of health of the special facilities for diagnosis, consultation and treatment open to him. It should be pointed out that facilities will include the examination of fœtal tissues for spirochætes and the making of Wassermann tests in the case of women who have had miscarriages
 - (ii) Every practitioner should be able, without payment, to obtain the laboratory assistance provided under the scheme. This provision is intended to be made gratuitously for the patient as well as for the practitioner
 - (iii) On application the practitioner should receive from the medical officer of health of the county or county boroughs or district, the apparatus required for collecting material for examination, with printed instructions for its use.
 - (iv) When necessary, he should be assisted in the collection of material
 - (v) Any patient brought by him to a clinic should be seen in consultation by the Medical Officer of the clinic.
 - (vi) Apart from such consultations the attendance of medical practitioners at the clinic should, so far as practicable, be encouraged
 - (vii) In suitable cases, when desired by the patient's own doctor, salvarsan or its substitutes should be administered by the Medical Officer of the clinic, subsequent treatment being conducted by the practitioner on systematic lines laid down at the consultation
 - (viii) Under certain conditions the Medical Officer of the Clinic will supply salvarsan or its substitutes for administration by the medical practitioner to his own patients

The relation of the general practitioner to the clinic is subject to the general rule laid down in the paragraph from the Royal Commission's Report to the effect that no patient must be refused treatment, or hindered in the receipt of treatment."

Not long after the 1916 regulations and recommendations had been issued the authorities agreed that in cases in which it was necessary, the travelling expenses of patients to the nearest clinic could be paid. This is a concession which needs to be more widely known, occasionally, particularly when a mother and child or children need to attend, it may make all the difference between regular treatment and default.

Such then were the conditions under which the Venereal Diseases Scheme began. Many clinics were attached to voluntary hospitals, in a minority of cases "*ad hoc*" clinics were established by local authorities.

VENEREAL DISEASES IN CHILDREN

Having considered the plans set up to control venereal diseases in this country, it will be of interest to try and appreciate the problems as they were presented at

that time, and to estimate the results of the application and adaptations of those plans

As has been stated, the statutory venereal diseases are syphilis, gonorrhœa, and soft chancre, a case of soft chancre in a child in this country would be a rarity, and it is the effects of syphilitic and gonorrhœal infections in childhood that will be dealt with now

Among evidence submitted to the Royal Commission was much that dealt with the effects of these infections in children

GONORRHŒA—The two clinical conditions arising from gonococcal infections in children are gonorrhœal ophthalmia in the newly born and gonorrhœal vulvo-vaginitis in female children below the age of puberty, the former is of course the more serious condition, accounting, as it did, for much of the blindness and impaired vision met with in infancy and childhood.

Ophthalmia neonatorum—The realization of the severe results of purulent ophthalmia in the newly born had led to the 1914 regulation making the notification of ophthalmia neonatorum obligatory on all medical practitioners and midwives, although before this many local authorities had included the condition in the local list of diseases notifiable under the Infectious Disease (Notification) Act. Some figures were available, but the most telling evidence given to the Royal Commission was that of N. Bishop Harman who, in his own words, "had oversight of a number of London blind schools," and who reported the results of investigation into the cases of 1,100 blind and partially blind children. Basing his diagnosis on the character of the damage done, the associated symptoms and the history of the case, he found that 24.35 per cent. of these children owed their blindness or impaired vision to ophthalmia neonatorum and, although bacteriological evidence was lacking, the presumptive evidence was that the responsible organism had been the gonococcus.

Vulvo-vaginitis—No figures were available to give reliable information on the prevalence of gonococcal vulvo-vaginitis in female children. Evidence was given that the condition was "frequently" found in girls below the age of fourteen years in children's hospitals and rescue homes and the usual list of possible infecting agents was given, the difficulties and tediousness of the treatment then available were emphasized.

SYPHILIS—In the nineteenth century the work of Fournier and of Hutchinson had stressed the gravity of syphilitic infection in relation to marriage, to the family and to social conditions, and also the value of treatment of the parents in the prevention of congenital syphilis. To quote Fournier's statement made over thirty years before (1881)—"The essential condition to be fulfilled by all syphilitic subjects aspiring to marriage, is contained in rigorous specific treatment—a treatment sufficient to confer a relatively complete immunity from the numerous and various dangers which syphilis brings into marriage." Nevertheless, at the time of inquiry, the Royal Commission found the facilities for the hospital treatment of venereal diseases in this country inadequate, and indeed some hospitals, by their statutes, could not admit patients suffering from venereal diseases. Treatment by salvarsan or its substitutes was too new to be general, and it is not therefore surprising that the picture given of the effects of syphilis in infancy and childhood

was gloomy. The two tables below will serve as examples, in the first the figures were supplied by Dr F W Mott, FRS, and in the second by Mr Bishop Harman.

TABLE I
FAMILIES OF 34 SYPHILITIC MOTHERS

<i>Mothers</i>	<i>Pregnancies</i>	<i>Premature births, still-births and deaths in early infancy</i>	<i>Children seriously diseased</i>	<i>Children apparently healthy</i>
34	175	104	41	30

TABLE II
(Records of 150 families in each of which one or more children presented definite signs of inherited syphilis)

<i>Families</i>	<i>Pregnancies</i>	<i>Miscarriages and still-births</i>	<i>Infant deaths</i>	<i>Children alive but diseased</i>	<i>Children alive and healthy</i>
150	1,001	172	229	390	210

As a comparison, Mr Harman investigated the family history of 150 "average" women attending the West London Hospital—any woman known to have a syphilitic history was excluded. The result was as follows—

<i>Families</i>	<i>Pregnancies</i>	<i>Miscarriages and still-births</i>	<i>Infant deaths</i>	<i>Healthy children</i>
150	826	78	94	654

Referring to the investigation of the 1,100 children attending the blind schools, 31.2 per cent were found to be blind or to be suffering from impaired vision as a result of congenital syphilis, whilst other evidence showed that the disease was responsible for 7.21 per cent of acquired deafness in 845 children attending the London County Council Deaf Schools.

PROGRESS AND ADAPTATION OF THE SCHEME

By 1923 there were in England and Wales 191 treatment centres, in Scotland 36, figures which have now risen to 228 and 51 respectively.

In 1929, when the Local Government Act came into force, a great deal of the control of the central authority passed into the hands of the Councils of Counties and County Boroughs, and a block grant which allowed for expenses incurred replaced the 75 per cent of cost formerly paid by the central authority.

At the time the clinics began, this country was facing problems similar to those it faces to-day, and, for lack of anything better, many of the early clinics were housed in premises far from satisfactory. On the part of some authorities and hospitals there was, too, an attitude that for these "unpleasant" diseases and patients anything was good enough. There has been gradual but steady improvement in clinic buildings, in the timing of clinics to suit the needs of patients, and in the staffing of clinics.

ANTE-NATAL WORK

Venereal disease clinics in hospitals or "*ad hoc*" clinics do not, however, cover the preventive side of the work, and it is in this, from the point of view of children the most important side, that the help and cooperation of others is vital. Of particular value is the work of all who have the care of pregnant women, whether private practitioner or medical officer in charge of an ante-natal clinic.

Many practitioners now send any patient suffering from a vaginal discharge for bacteriological examination and any patient with a suspicious obstetric history for investigation to venereal diseases clinics. In the bigger centres it is possible to set aside one session for married women and children, and so overcome the objections that some might have to attending such clinics. With increasing knowledge such objections are becoming less frequent and, provided the venereal diseases clinic is well conducted, protest on the part of any patient is exceptional.

A circular from the Ministry of Health in April 1935, with particular reference to congenital syphilis, stressed the importance of cooperation between the venereal diseases, maternity and child welfare, and school medical services and private practitioners, in this same circular the point was emphasized of the tendency of mothers to default after child-birth, and the influence that could be exerted by giving a reasonable explanation of the disease and of the necessity for prolonged treatment.

Other matters treated in this circular were the privileged nature of confidential communications between medical practitioners, the need for provision of following up defaulters, and the facilities for ensuring that patients were not deterred from attending by the cost of travelling to the clinic. Again, in 1937, a circular on "The Prevention of Blindness" devoted a short section to venereal diseases, to the value of preventive measures and of treatment.

In a few ante-natal clinics the diagnosis and treatment of venereal diseases is undertaken very successfully, but the organization of such a double-purpose clinic needs care and discrimination, or it may result in the ante-natal clinic being shunned by other patients.

Increasing numbers of ante-natal clinics are adopting the practice of taking blood for Wassermann test as a routine, a procedure that has everything to commend it if all the possible pitfalls are kept in mind. The taking of blood is a simple procedure but must be done carefully, so that the specimen reaches the experienced pathologist in good condition.

There are, too, conditions which may give rise to false positive reactions, whilst of course a negative Wassermann does not necessarily mean freedom from syphilitic infection. A diagnosis of syphilis or even a suggestion of syphilis on one positive Wassermann, with nothing else to support it, is unjustifiable, and in such circumstances the positive Wassermann should be taken only as an indication for further investigation.

HOSTELS FOR UNMARRIED INFECTED GIRLS

In some towns, hostels for unmarried pregnant girls suffering from venereal disease have been instituted by voluntary organizations, and these are eligible for

a grant under the Venereal Diseases Scheme. The girls receive treatment during pregnancy, and in many cases stay, with their babies, for three months or more after delivery. Such patients present a variety of social problems, perhaps the greatest of which is what can best be done for the child, often, happily, these children are born free of infection, but in cases in which the mother is syphilitic and has only come under treatment comparatively late in pregnancy, the child needs careful observation for at least five years, adoption is ruled out in such cases, foster mothers are unwilling to take a child needing to be brought to hospital periodically for blood tests, the girl is often unable to keep the child with her, and the knowledge and skill of the best of social workers are taxed to the uttermost.

THE CHILD OF SCHOOL AGE

Many difficulties are encountered with regard to the attendance for treatment of the child of school age, this is especially true of the congenital syphilitic, whose treatment is long and, at least in the early stages, bitterly resented by any child. Most parents will cooperate but there are always those who, from an inability to take the long view or, less frequently, from carelessness or sheer neglect, do not bring a child for necessary treatment. Such cases present a problem requiring careful and diplomatic handling, but valuable help can be obtained from the school medical officer and from the workers of Children's Care Committees. In cases in which there is gross neglect or the child is in an infective condition, admission to hospital is the best solution. The London County Council has at White Oak, Swanley, accommodation for children suffering from interstitial keratitis, where the children can remain under treatment, during which time their education is continued, whilst beds for other cases are provided at the London County Council hospital at Carshalton.

THE SOCIAL SERVICE WORKER OR ALMONER IN THE VD CLINIC

There seems to be still a great deal of misconception as to the work of hospital almoners, the name is perhaps unfortunate and savours either of "charitable help to the deserving poor" or of a concern for hospital finance involving a "means test" for every patient.

In the venereal diseases department there is no questioning as to patients' means and the almoner is there to help the patient, and, to a scarcely less extent, does help the medical officer. She is there primarily to smooth out difficulties which may interfere with the continuity of the patients' treatment, to follow up defaulters, and help in what has always been an important part of the work of a venereal diseases department, that is, trying to get contacts of infected patients to go for examination and treatment.

The specialized and practical knowledge of a hospital almoner is in no instance of more value than in the case of children, whether infected and needing treatment themselves, or the children of mothers under treatment. The value of the work has been recognized by the Minister of Health, and a circular of 1943 points out the advantages of employing almoners on the staff of venereal disease clinics and that extra expenditure incurred would rank for Exchequer grant.

One of the best effects of the much criticized 33B Regulation is that it has brought the social problems of venereal diseases squarely before many who knew little or nothing of them before. A great deal has been heard of "contact tracing" recently and it is, by many, regarded as something new and unthought of before. It may be of interest to quote an extract from the Report of the Chief Medical Officer of the Ministry of Health, 1922 —

"The importance of tracing contacts cannot be too strongly emphasized. A syphilitic child implies a syphilitic mother and the prospect of more syphilitic children in that family, unless the mother is treated. Most valuable work has been done in some centres by using the clue afforded by one infected member of a family to secure the treatment of all members, and no Venereal Diseases Scheme can be considered complete unless it contains provision for this valuable branch of preventive medicine. It is the duty of everyone who has to treat a case of venereal disease, whether at a Venereal Disease Treatment Centre, a Maternity and Child Welfare Centre, or in private practice, to ask himself if this patient's disease means disease in others, and if it does, to secure the treatment of those others by whatever means appear suitable."

GENERAL PRACTITIONER SERVICE

A further war-time development of the Venereal Diseases Scheme has been the institution of a practitioner service for the treatment of venereal diseases in rural areas where distance or transport difficulties make attendance at a clinic impracticable.

The details are to be found in a Ministry of Health circular (Circular 2226, 1940) it was suggested that County Councils and County Borough Councils should consider what areas were in need of such a service, and how many practitioners would be required. Practitioners who wished to serve under this plan were required to have had a certain minimum of experience or to be willing to take advantage of training facilities, equipment and drugs were provided and a scale of fees was laid down.

Expenditure incurred on this service by local authorities, during the war, ranks for Exchequer grant.

RESULTS

Gonococcal ophthalmia neonatorum — The high percentage of blindness due to gonococcal ophthalmia neonatorum given in the Report of the Royal Commission, proved so startling that the figure goes on being quoted, but in reality the incidence of blindness and impaired vision has declined, and, of late years, rapidly declined.

In 1921 in England and Wales, there were 7 cases of blindness and 82 cases of impaired vision out of 4,555 cases of ophthalmia neonatorum notified by 83 local authorities, whereas in the four years 1940, 1941, 1942, and 1943, only 7 infants became blind and 31 had impaired vision.

The following table illustrates the rapid rate of decline —

<i>Metropolitan boroughs</i>	<i>Impaired vision</i> (per 100,000 births)	<i>Blind</i> (per 100,000 births)
1924-1933	10.7	1.0
1934-1943	1.6	0.4
<i>County boroughs</i>	<i>Impaired vision</i> (per 100,000 births)	<i>Blind</i> (per 100,000 births)
1924-1933	18.68	2.2
1934-1943	4.5	0.9

The success achieved is the work of many; it is the result of improved ante-natal care and more consistent use of prophylactic measures at the time of birth, and of modern methods of treatment, both

for the pregnant woman suffering from gonorrhœa, as well as for the condition of gonococcal ophthalmia when it does occur

Gonococcal vulvo-vaginitis — No figures are available for the incidence of gonococcal vulvo-vaginitis in children. Epidemics in hospitals and institutions are now extremely rare, and the experience of medical officers at different clinics is variable. Some four months ago at the Royal Free Hospital, in the space of ten days, three children with gonococcal vulvo-vaginitis were seen, since then there has not been a single case. Two were admitted and both were found resistant to sulphonamide treatment, and were treated with penicillin, the third case had, for lack of a bed, to be transferred. In neither of the cases admitted could the source of infection be found.

With the cutting short of the period of infectiveness in adults by sulphonamide treatment, and still more so by penicillin, these cases will be expected to become less frequent.

Congenital syphilis — Since the "peak" years at the end of the last war, the incidence of early syphilis in adults declined until the years of this war when, as in all wars, it again rose. Figures from the clinics in England and Wales showed a decline, too, in the numbers of congenital syphilis, but since 1940 these have again risen.

In 1917, the death rate of children under one year certified as due to syphilis per 1,000 live births was 2.03, in 1927, 0.77, and in 1937, 0.23. It is, of course, recognized that certification does not cover all deaths from

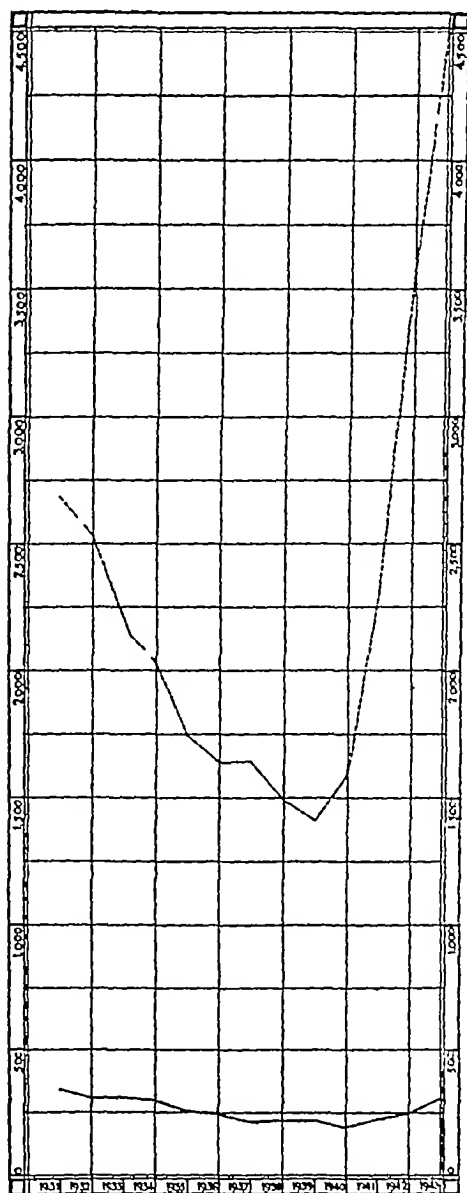


FIG 1

----- Indicates recent syphilis in women
 ————— " congenital syphilis (under one year)

syphilis, but the figures do give a comparative standard.

During the ten years 1934 to 1943, the numbers of cases of congenital syphilis, under one year, dealt with for the first time at clinics were as follows —

1934	296	1939	217
1935	251	1940	191
1936	241	1941	223
1937	211	1942	245
1938	216	1943	310

The accompanying graph (fig 1) shows the relation of cases of congenital syphilis under one year to those of recent syphilis in women (recent syphilis means syphilis of less than one year's duration)

The marked increase in the incidence of syphilis in women cannot fail to give rise to anxiety, but women do now attend the clinics, whereas during the 1914-18 war few clinics were open, and there was far more ignorance and fear than exist at present. Nevertheless, the lesson to be learned is obvious to continue to give to the public the information it should have on venereal diseases, to provide all possible facilities for diagnosis and treatment and, by careful choice of staff and consideration for patients, to keep the patient under treatment for the requisite time

PENICILLIN

Penicillin is now available for the treatment of venereal diseases. In gonorrhœa the results are excellent and the treatment in adults does not involve hospitalization, in children it would still seem to be advisable to admit the patient to the wards, if possible. The two cases referred to above were both given 50,000 units and local treatment was limited to simple swabbing; sulphonamide treatment had already made unnecessary the douches and applications, so undesirable and so ineffective, which formed the chief part of older treatments

Syphilis — Much work has been carried out in America and an increasing amount in this country, with penicillin in the treatment of syphilis, but some time must elapse before its value can be estimated. The effect of penicillin in early acute syphilis, is to cause rapid disappearance of spirochætes from surface lesions, and rapid healing of lesions, but syphilis is characterized by its chronicity and its tendency to relapse, and it would be extremely undesirable to discard old weapons before having thoroughly tried the new one

With regard to pregnant women and penicillin treatment, it has been recommended that pregnant women suffering from gonorrhœa should not be given penicillin but should be treated with sulphonamides. This is to prevent the possible effect of making undetectable a coincident syphilitic infection, and so exposing the child to the danger of congenital syphilis

References

- Fournier, A. (1881) "Syphilis and Marriage" (translated by A. Lingard)
Lancet (1899) 2, 847
 — (1902) 2, 953
 Public Health (Venereal Diseases) Regulations (1916) London
 Royal Commission on Venereal Diseases (1916). London.

Within a few seconds the jaw became clenched, the abdomen board-like, and the respirations gasping. Slight risus sardonicus with furrowing of the eyebrows was present. No wound, apart from tiny scratches on the knees, could be found, but the teeth were carious and the breath fetid. Culture of an extracted tooth and of the stools was negative for tetanus bacilli, and the cerebro-spinal fluid was clear. Within a few hours, spasms of the neck and back occurred, and the following morning clonic spasms of the legs. A double intravenous drip was started, one bottle containing 5 per cent glucose alternating with normal saline (to keep the vein open) and the other pentothal sodium, 1 gm. to 500 c.c.m. normal saline, to control the fits. The bottles were attached to a Y tube, the stem of which ran into a common canula. The glucose-saline drip was continuous, at a rate sufficient to keep the vein from closing, and when spasms occurred this tube was clipped off and pentothal sodium run in at the rate of about forty drops per minute. This was usually followed within a few minutes by relaxation and sleep, which lasted for three to four hours. In view of the frequency of the spasms the patient was kept almost continuously under anaesthesia for the first three days, being allowed to drink a little on regaining consciousness and then being anaesthetized again. With a view to minimization of any pulmonary infection, 1 grain of soluble sulphapyridine was added to each 500 c.c.m. of glucose or saline. On the second treatment day moist sounds were present over both lungs and froth was exhaled. 1/150 grain of atropine was given, followed by 1/120 grain daily, as required, for the next three days. The irritating effect of the pentothal necessitated cutting down on both ankle and basilic veins. For the first eight days 100,000 units of anti-tetanus serum were given daily by the intravenous route. Improvement set in on the eighth day of treatment, the spasms becoming less severe and the periods of consciousness longer. On the sixth day pentothal sodium was stopped, for fear of possible hepatic damage, and avertin and paraldehyde in soya oil rectally and nembutal by mouth were tried for twenty-four hours. paraldehyde in dosage of 240 minims proved the most useful. Intravenous drip was stopped on the eleventh day and recovery was uneventful, the boy being discharged one month after admission. It is claimed for the method that it can serve for fluid, food, drugs and serum, nursing is considerably eased, and there is minimum manipulation of the patient.

PENICILLIN IN VINCENT'S INFECTION

A REPORT of the success obtained by the use of penicillin-agar pastilles in the treatment of fusospirochaetal infection of the mouth (Vincent's

type) is given by P. Greey and Surg. Lt. J. B. Macdonald (*Canadian Medical Association Journal*, April 1945, 52, 327). The pastilles are prepared by placing 200 c.c.m. of distilled water in a flask and adding 8 gm. of agar. The mixture is autoclaved for thirty minutes and then, while hot, filtered through non-absorbent wool and the agar collected in a flask, which is placed in a water bath at 50 to 55° C. When cooled to about 50° C. the required amount of penicillin is added, thoroughly mixed, and the molten mixture poured into a glass tube with a rubber stopper at the lower end. When firm setting has taken place the stopper is removed, the column of agar expelled by elevating one end and the cut into slices 0.5 cm. thick. If it is intended to store the pastilles for several weeks, butabate (n-butyl ester of p-hydroxybenzoic acid) can be added when mixing the distilled water and agar. Tests carried out to ascertain the keeping qualities of the pastilles showed that with a penicillin content of 400 units there was no loss after ten days' storage, but after twenty days storage the loss was about 50 per cent. In all the treated cases there was rapid elimination of the infecting organisms and prompt improvement in the clinical signs and symptoms, the clinical improvement usually being noted within twenty-four hours of starting treatment. The chief advantage claimed for the use of penicillin agar pastilles is that they persist in the mouth for at least four hours, during which time a bacteriostatic concentration of penicillin is maintained in the saliva. It was found that a single pastille containing 75 units of penicillin was sufficient to maintain a concentration of at least 0.3 units per c.c.m. saliva over a four-hour period. Tests of the urine of treated patients showed that the highest urinary concentration of penicillin in a four-hour period, during which a 10,000 unit agar pastille was in the mouth, was 0.4 unit per c.c.m. The use of penicillin incorporated in packs placed in the space between the teeth of patients with Vincent's infection is reported by Surg. Lt.-Cdr. R. Thornton and Surg. Lt. P. K. Dick (*British Dental Journal*, May 18, 1945, 78, 292). 100,000 units of penicillin sodium powder was triturated in a sterile mortar and 2 gm. of light magnesium oxide added, mixing for ten minutes to ensure even distribution. After ascertaining the number and size of packs required, one or two drops of pure olive oil were placed on a clean mixing block, and enough of the penicillin-magnesium oxide powder added to make a paste of the consistency of soft butter. Small wisps of cotton-wool were then incorporated to make the packs of requisite size. Strict asepsis is necessary. The report is a preliminary one but the results appear encouraging—patients were free of symptoms in twenty-four hours, the pain vanished, bleeding

decreased, and in severe cases a good night's sleep was obtained. Sloughs separated in thirty-six to forty-eight hours, and in four to five days the ulcers were epithelializing. Examination of microscopic slides at this time showed that the fuso-spirochætal symbiosis had disappeared. In no case was packing continued after five days. It was also found that the packs, when inserted in the areas of severe ulceration, acted as reservoirs, slowly liberating the penicillin into the mouth, so that lesions remote from the packed areas resolved.

INTRAVENOUS INJECTIONS OF ACETYLCHOLINE IN PAROXYSMAL TACHYCARDIA

On the basis of the success obtained by the experimental study of the hearts of rabbits and dogs under the influence of acetylcholine, M. Segers, J. Lequime and H. Denolin (*Presse Médicale*, May 12, 1945, 53, 242) have treated a series of seven patients with paroxysmal tachycardia by injections of 10 to 100 mgm. acetylcholine, dissolved in 2 to 10 c.cm. distilled water. The patient was placed in the dorsal decubitus position and, if he had not been previously treated, an initial dose of 20 mgm. was given. If the attack did not cease immediately, injections were repeated every three to four minutes, using, successively, doses of 40, 60, 80 and 100 mgm. The last-named dosage was never exceeded, the average active dosage in the seven cases being 10, 40, 50, 50, 70, 80 and 90 mgm. respectively. When attacks recurred the dose that had previously proved effective was immediately administered. The intravenous route was always employed as, owing to the rapid destruction of the drug by the blood and tissues, other routes of administration did not produce any appreciable reaction of the heart. When giving the injections care must be taken to avoid the entry of blood into the syringe, and the injections must be given as quickly as possible. While the patients were receiving their injections an electrocardiogram was taken in order to register the results. It was noted that the sinus activity was established with a fairly slow rhythm, frequently interrupted by extrasystoles, the beats became regular and accelerated rapidly, to regain normality in one or two minutes after the acceleration. In all cases the attacks were stopped promptly in less than thirty seconds after the injection, the usual time being ten to fifteen seconds. Secondary reactions were inconstant, and were always of brief duration. In some instances there were fits of coughing, nausea and feeling of faintness. Three of the patients were ambulant and all returned home without incident. Three others were unable to move during the attacks, which involved rapid fall in blood pressure with

dyspnoea and asthenia nevertheless, these patients tolerated the injections well. All the patients were of fairly advanced age, a fact which the authors state speaks well for the method, as it is precisely in such patients that the arrest of acceleration is most difficult. In conclusion, it is stated that acetylcholine appears to be superior to other vagomimetics in view of the greater efficacy, the good tolerance, and the fact that the rapid destruction of the drug in the organism permits quick repetition with higher dosage should the first administration fail.

PUNCH ACTINOMYCOSIS

An interesting case of actinomycosis of a metacarpal bone following a punch injury is recorded by H. Jackson Burrows (*British Journal of Surgery*, April 1945, 32, 506) —

An Irish able seaman assaulted a fellow sailor and broke one of his teeth. The broken stump made a clean-cut wound over the head of the fourth right metacarpal bone, extending down to, but not dividing, the extensor tendon. By the sixteenth day recovery appeared to be complete, except for slight swelling of the knuckle. Five days later the wound broke down and discharged for nine days; twice subsequently a fluctuating swelling was incised. Finally, ten weeks after the original injury, the patient was admitted to an orthopaedic centre where X-rays showed rarefaction of the medial half of the fourth right metacarpal bone with a cuff of subperiosteal bone covering the distal two-thirds of the shaft. Three weeks later an abscess pointed at the distal palmar crease, and on incision yielded pus containing pale yellow granules which were found to contain the mycelium of actinomycosis. Potassium iodide was then administered and 115 days after the injury was sustained the X-rays of the metacarpal bone were almost normal and there was full function of the hand. When last seen, practically a year after the incident, the clinical condition was satisfactory.

Two other cases of actinomycosis of the hand following a punch injury have been recorded. In all three cases a sinus was, or had been, present by the time they were diagnosed ten weeks to six months after the injury; the signs were those of chronic subcutaneous infection with suppuration and sinus formation. In the two cases X-rayed, the changes were those of a small cavity in the affected bone with irregular subperiosteal thickening; the Wassermann reaction was negative. In two cases the diagnosis was made from examination of the pus, in the third it was made from an examination of the affected finger that had been amputated as a result of a diagnosis of sarcoma. From the point of view of differential diagnosis, sarcoma of the bones of the hand is rare, and routine examination of the pus from a sinus should show the presence of the fungus. Whilst in the case recorded, examination of the mouth of the patient's adversary six months after the incident did not reveal the presence of actinomycosis, it is known that actinomycetes of, or resembling, pathogenic types are found in the mouths of apparently healthy individuals, so that there is a strong presumption that in all three cases the infection was acquired by implantation of the fungus from the adversary's tooth into the wound which it made.

REVIEWS OF BOOKS

The Premature Baby By V MARY CROSSE, M D, D P H, M M S A, D R C O G London J & A Churchill Ltd, 1945 With 14 illustrations Pp viii and 156 Price 10s 6d

Those who read the article on this subject by Dr Mary Crosse in a recent issue of *The Practitioner* will be glad to have a considerably larger version of her views made available in this new volume. That the subject is of first-rate importance is clearly emphasized by Prof L G Parsons in a foreword. Deaths in the first month of life have not shown the striking reduction achieved in the remainder of the first year of life during this century. Half the babies dying in the first month have been born prematurely. Hence anything which will assist in the better management of the premature baby is a real contribution to the saving of infant life. Dr Crosse sets out what she has done in Birmingham in the past fourteen years. Her methods are essentially simple, suitable for the home as well as for the hospital, although she stresses the relative ease of transport in special baskets. The results obtained by Dr Crosse are certainly better than those published from any other centre in this country, and that alone justifies a close study of this book. It is full of practical information, well set out and with a good index. All practitioners who still do midwifery should possess a copy, and it will also be read with profit by obstetricians and paediatricians.

Human Embryology (Prenatal Development of Form and Function) By W J HAMILTON, M D, D Sc, F R S E, J D BOYD, M Sc, M D, and H W MOSSMAN, M S, Ph D Cambridge W Heffer & Sons Ltd, 1945 Pp viii and 366 Figures 364 Price 31s 6d

A GENERATION ago a somewhat scanty knowledge of embryology was considered sufficient for the student of medicine, but during recent years it has been increasingly recognized that a proper understanding of the way in which the body has grown and developed is essential to any useful comprehension of its structure and function. To gain this understanding will not add to the already grievous burden of the modern medical student but will lighten his load by explaining much that is otherwise inexplicable in his pre-clinical and clinical studies. As the authors of this excellent book themselves point out, a sound knowledge of embryology cannot be obtained solely from a textbook, and the examination of serial sections of mammalian and, best of all,

human embryos is necessary fully to reveal those unfolding processes which result in the formation of the adult body. Even with such material at his command, however, the student still needs a trustworthy guide, and the present book by its clearly written text and the profusion and beauty of its illustrations, eminently supplies his need. Many will welcome the lucid and up-to-date account of the microscopic anatomy and physiology of the ovarian and menstrual cycles, the beautiful photographs and drawings which illustrate the formation of the germ layers and the development of the fetal membranes, placenta and decidua—all subjects of primary importance to the medical student. The chapters dealing with the cardiovascular, the genito-urinary, and the nervous systems are perhaps the richest sections of the book. The final chapter is a skilfully compiled résumé of comparative vertebrate development which will meet the needs of those—and there should be many—who have the interest and opportunity to study those processes in lower forms which throw so much light on our own developmental history. For the advanced student and those who, for the solution of clinical and other problems, will wish to consult the literature of some particular subject, a full bibliography is provided at the end of each chapter. The compilation of this, in itself, must have entailed a vast amount of painstaking toil, but it greatly adds to the value of an already valuable book. The book is the product of an Anglo-American alliance, in itself a happy augury, and is an index of that collaboration which in medical science has had its triumphs no less than in other fields. Mr A K. Maxwell has enhanced his already high reputation as an anatomical artist, and the publishers are to be congratulated on the format of their production.

The Examination of Reflexes By ROBERT WARTENBERG, M D With a Foreword by FOSTER KENNEDY, M D Chicago The Year Book Publishers, Inc, 1945 Pp xii and 222 Figures 7 Price \$2 50

PRACTICALLY two hundred and fifty reflexes have been described, and this number is still increasing, as seventy-six new ones were reported in the literature between 1918 and 1935. Whilst only a minority of these have gained general currency, the position is most confusing for the neurologist, especially as many of the so-called "new" reflexes are only old ones to which a new name (usually the author's) has been attached. In this monograph, put together from articles which have appeared in the

Archives of Neurology and Psychiatry, the author has attempted to bring order out of chaos. It is a critical evaluation of the claims that have been advanced for the existence of the vast majority of the reflexes that have been described. The extensive bibliography (there are more than 430 references) is culled almost exclusively from continental journals. This is not a book for the general reader; but the specialist, or the post-graduate worker for a higher examination, will find it a valuable guide to a hitherto neglected subject.

Rebel Without a Cause By ROBERT M LINDNER, PH D London Research Books, Ltd, 1945 Pp xii and 259 Price 21s

THIS is an important contribution to the knowledge of the psychology of crime. Its subtitle—"The Hypnoanalysis of a Criminal Psychopath"—indicates what it is about and it is commended in an introduction by the well-known Harvard pair—Prof Sheldon Glueck and Eleanor T Glueck. The subject, called Harold, was given forty-six sessions of analysis under hypnosis and at the end of that time his complicated history of crime was unravelled, both for himself and for the reader. Probably up to about one-fifth of the inmates of prisons fall into the group of psychopathic personalities. There is no simple cure for them and elaborate investigation and study such as is recorded in this book can scarcely be applied on a wide scale. Nevertheless, whatever may be the expert view on hypnoanalysis, Dr Lindner has clearly demonstrated that it is something far better than what the Gluecks term "the almost bankrupt procedure now employed by society." This is a book for all those directly interested in the prevention of crime.

Medicine By GEORGE LUNTZ, M.R.C.S, L.R.C.P London Robert Ross & Co Ltd, 1945 Pp 64 Price 2s 6d

IN this little book, a recent issue of the Ross Careers Books Series, detailed information is given on how to prepare for a medical career. Not only does the author give particulars of the medical curriculum and fees at the different medical schools in England, Scotland, Ireland and Wales, but there is also a useful chapter on the Health Services at home, abroad and in the Forces, and their financial aspects. Post-graduate medical education and research are the subjects of another chapter, and yet another is devoted to the examining boards, the necessary subjects and the fees entailed. The book has been well and carefully prepared, and should prove of value to those about to take up medicine as a career or wishing to qualify for appointments in the Health Services.

NEW EDITIONS

IN *The Medical Directory*, 1945 (J & A. Churchill, 63s) the numerical summary of the medical profession continues to show an increase, although the actual increment (750 as compared with 1513 for 1944) is the lowest since the year 1937. Temporarily registered medical practitioners now total 3,550, an increase of 868 on the figure for 1944. The general make-up and production show no variation. New features include the omission of the late list of new names and changes of address, no doubt on account of the late appearance of the directory—or maybe due to the more prompt supply of information—the appearance of the Chartered Society of Physiotherapy for the first time under its new title, and the inclusion in the list of registered chiropodists of members in South Africa, Eire and Belgium.

THE sixth edition of *An Index of Differential Diagnosis of Main Symptoms*, by various writers, edited by HERBERT FRENCH, C.V.O., C.B.E., M.D., F.R.C.P., and ARTHUR H. DOUTHWAITE, M.D., F.R.C.P. (John Wright & Sons Ltd, 84s) appears after a somewhat stormy production period due to enemy action and war-time difficulties. Several changes are noted among the list of contributors: death has removed the well-known names of Sir Arthur Hurst, Sir Archibald Garrod, Professor John Eyre, Mr Hastings Gilford and Mr Jocelyn Swan, and Sir Herbert Lightfoot Eason and Professor George E. Gask have retired. Their places have been taken by leading experts in the different branches of medicine and surgery, and the sixth edition also marks the collaboration of A. H. Douthwaite as assistant editor. Brought up to date in every section and richly illustrated, containing in all 798 figures, the new edition will be a valuable addition to the armamentarium of all medical practitioners.

THE twelfth edition of *Hey Groves' Synopsis of Surgery*, edited by CECIL P. G. WAKELEY, C.B., D.Sc., F.R.C.S., F.R.S.E., F.A.C.S., F.R.A.C.S. (John Wright & Sons Ltd, 25s) contains as a frontispiece a photograph of the original author, whose death occurred at the end of last year, when the work of revision was almost completed. Although only three years have elapsed since the appearance of the eleventh edition, considerable revision has been undertaken, and among the new additions are the use of penicillin in the treatment of gonorrhoea and wound infection, and new methods of radium therapy. The use of Trueta's closed plaster technique in conjunction with sulphonamides is described in the chapter on wounds.

NOTES AND PREPARATIONS

NEW PREPARATIONS

MENOPAX ANTI-PRURITIC CREAM (amethocaine 0.5 per cent, benzocaine 5 per cent., diethylstilboestrol 0.1 per cent., zinc oxide 10 per cent., camphor 2 per cent., terpineol 1 per cent., emulgent wax 30 per cent.) has been prepared for the local treatment of pruritus vulvæ and allied conditions. The manufacturers are Clinical Products Ltd, Richmond, Surrey, by whom the cream is issued in 1 ounce tubes or jars, price 4s 10½d, and in 8 ounce packs for dispensing, price 28s 6½d, both inclusive of purchase tax.

METHYL THIOURACIL (Organon) is now available in bottles of 100, 500 and 1000 tablets of 50 mgm. and 200 mgm. The manufacturers are Organon Laboratories Ltd, Brettenham House, Lancaster Place, London, W C 2, from whom further particulars can be obtained.

'WELLCOME' INJECTION OF LIVER EXTRACT—This product, which is stated to be prepared by a special process which conserves the active principles whilst eliminating inert or antigenic substances, is available in ampoules of 2 c.cm. in boxes of 6, price 6s 8d and boxes of 25, price 25s (exempt from purchase tax). The manufacturers are Burroughs Wellcome & Co., 183-193 Euston Road, London, N W 1.

BOOTS PURE DRUG CO. LTD

SIR JACK DRUMMOND, F.R.S., D.Sc., F.I.C., Chief Scientific Adviser to the Ministry of Food, has been appointed Director in charge of Messrs Boots scientific research. Although he has resigned the Chair of Biochemistry at University College, London, Sir Jack Drummond will not take up his new appointment until there is an improvement in the food situation.

PARKINSON'S DISEASE

A "PERSONAL" announcement which has appeared recently in the *Times* and the *Daily Telegraph* covers a scheme by which it is proposed to form a research unit at the National Hospital, Queen Square, to investigate the cause and possible cure of Parkinson's disease. A fund has been started for this purpose, the writer of the announcement heading the subscription list with a sum of one hundred guineas, the scheme is to raise at least another 2,000 guineas to begin with. Practitioners may be able to bring this appeal to the notice of patients or their relatives. Anyone interested should communicate with Mr E. Teller, Ridgeland, Bidborough, Kent.

THE CENTRAL COUNCIL FOR HEALTH EDUCATION

AN amusing and attractive new series of leaflets

is being issued by the Council for Health Education, the first three of which deal with the subjects of lice, infant feeding, and the prevention of spread of respiratory infection. The cover designs are the work of Fougasse who has also designed an intriguing poster on the vexed question of spitting. Copies of the poster are available, price 6d each, 25s for fifty and 35s for one hundred, and of the leaflets, price 2d each, 8s for one hundred and £3 5s per thousand. Application should be made to the Central Council for Health Education, Tavistock House, Tavistock Square, London, W C 1.

JOURNAL OF THE INDIAN ARMY MEDICAL CORPS

THE first number of this journal, which is edited by Colonel D. R. Thapar, O.B.E., M.D., opens with an inaugural message from Lieutenant General Wilson, C.B., C.B.E., M.C., K.H.S., Director of Medical Services in India. The journal will be published twice yearly, and the annual subscription rate is Rs 5 (approx. 5s), payable in advance. Communications concerning subscriptions, etc. should be addressed to Headquarters, I.A.M.C., Poona, India.

BRITISH ACHIEVEMENT IN THE ART OF HEALING

THIS is number 4 of the Achievement Books, edited by Noel Carrington. The present issue is by John Langdon-Davies, and deals, among other subjects, with the evacuation and treatment of wounded, the psychiatric measures employed to endeavour to fit "round pegs in round holes," blood transfusion, penicillin, M & B 693, the closed plaster technique, and rehabilitation. The book, which is most generously illustrated, is published by the Pilot Press Ltd., 45 Great Russell Street, London, W C 1, price 2s 6d.

CONTENTS FOR AUGUST, 1945

ORTHOPÆDICS

- Rest in Disabilities of the Locomotor System* By Professor Harry Platt, M.D., M.S., F.R.C.S., F.A.C.S.
Congenital Dislocation of the Hip By George Perkins, M.C., M.Ch., F.R.C.S.
Mal-union of Fractures By R. Bromhead, M.B., Ch.B., F.R.C.S.
Sciatica as an Orthopaedic Problem By Kenneth H. Pridie, M.B., F.R.C.S.
Osteoarthritis as an Orthopaedic Problem By A. M. Hendry, M.B., F.R.C.S.
Child Health XIV—The Deaf Child By A. H. Gale, D.M., D.P.H.

THE PRACTITIONER

No 926

AUGUST, 1945

Volume 155

REST IN DISABILITIES OF THE LOCOMOTOR SYSTEM

By HARRY PLATT, M.D., M.S., F.R.C.S., F.A.C.S.

Professor of Orthopædic Surgery, University of Manchester, Consultant Adviser in Orthopædic Surgery, Ministry of Health (Emergency Medical Service)

REST is one of the oldest forms of therapy. Its prescription was implicit in the practice of the Hippocratic school, but always with due regard to its possible misuse. In the early years of the twentieth century, every student in the medical schools of Great Britain was urged to read a remarkable, but now almost forgotten, book, "Rest and Pain" (1863) by the Guy's surgeon, John Hilton (1807-1878), and many did so with pleasure and lasting benefit. Hilton believed that the prime function of the surgeon was to remove or mitigate the effects of the obstacles to the natural processes of repair. In his emphasis on this teaching he followed in the wake of Hippocrates, Ambrose Pare and John Hunter. Hilton described, from a wealth of clinical experience, the rôle of rest in inflammatory diseases of joints. But rest had to be prescribed with care and carried out with precision. Active movements, in the form of a planned programme at any rate, appeared to have no conspicuous place in his therapeutic repertoire. He also taught that the indications for rest were often made clear to the surgeon by the occurrence of pain. Pain, to Hilton, was a diagnostic sign of great significance, and its distribution, when carefully analysed, led to the discovery of the site of disease. In a subsequent generation, the leading apostle of the doctrine of rest was Hugh Owen Thomas (1834-1891). We are less remote from the influence of his personal teaching, for it was expounded and illuminated in our own day by his nephew and pupil, the greatest master of orthopædic surgery of modern times—Robert Jones (1858-1933).

Rest may be prescribed in the form of (1) *general* or bodily rest under conditions conducive to peace of mind, or (2) *local* rest applied to the affected region. In actual practice, in the treatment of the majority of affections of the locomotor system, rest is generally achieved by the use of various types of mechanical support or fixation. Obviously, no form of therapy can be considered in isolation, but it is convenient to discuss separately the application of rest, support and fixation.

USE OF LOCAL REST, SUPPORT AND FIXATION

Rest—The rôle of rest may be illustrated in the treatment of the following conditions —

- (1) In the early stages of the repair of aseptic injuries of soft tissues and bone. Here, rest has two objectives—the relief of pain, and the promotion of healing by the removal of harmful stresses on young vascular connective tissue or procallus.
- (2) In the early stages of infected wounds, whether soft tissue injuries or compound fractures. The special value of rest in such circumstances is the discouragement of the spread of bacteria and toxins beyond the confines of the original lesion.
- (3) In inflammatory and destructive diseases of joints at different stages, in the early stage of acute suppurative arthritis, in tuberculous arthritis during the stage of onset, of evolution, and of healing; in rheumatoid and allied types of arthritis in the acute stage. In joint disease, rest not only relieves pain but allays muscle spasm, which, if allowed to be perpetuated, may be succeeded by fixed contracture.
- (4) In the early stages of certain types of paralysis—most notably in acute anterior poliomyelitis, for the relief of both pain and muscular spasm.

In all the conditions enumerated above, if for any cogent reason rest must be prolonged, it is essential that correct postures should be adopted for the affected parts. In general, this means the neutral or physiological rest position appropriate to each particular joint. In the wrist joint, for example, the neutral position which will ensure maximal grip of the fingers, is in precise terms 15° dorsiflexion and 3° ulnar adduction—in popular terms, the “cock-up” position. The digital joint must be rested in the position of slight flexion, the shoulder joint in abduction of the order of 45° with the arm in front of the plane of the shoulder and internally rotated, the elbow, in the right-angle position, but modified in accordance with the wishes of the patient. In the lower limb joints the neutral rest positions are—for the hip, 15° abduction and some 25° flexion, for the knee, extension, but not over-extension, and for the ankle, the right-angle position.

Mechanical support—Support is not only a convenient means of enforcing local rest but has its own special virtues. When applied to an injured part in the form of evenly distributed compression, the tendency to the spread of the œdema and hæmorrhage is checked. Support is always required to maintain a joint in the neutral rest position, to prohibit a particular arc of movement injurious to the healing process, or to prevent the prolonged over-stretching of a temporarily paralysed muscle or muscle group. The conventional methods of applying support involve the use of strapping, compression bandaging or splints (metal or plaster of Paris). The practical application of support may be illustrated in the following conditions —

Take, for example, such commonplace injuries as *strains* of the external lateral ligament of the ankle and of the internal lateral ligament of the knee. By strapping the ankle with the foot everted, compression can be applied to the injured ligament and at the same time restrict the movement of inversion, which is harmful. When

the patient is allowed to walk from the beginning—the conventional practice—should be observed that the rest imposed is relative, not absolute. This is an important principle in the treatment of all injuries of this type. Similarly, compression of the injured knee by a firm elastocrêpe bandage over layers of cotton-wool, controls the effusion and restricts mobility to the required degree. Here, again, the patient is encouraged to bear weight on the limb, but to avoid stress in the injured ligament by walking with an intoeing gait and using very short steps.

In *infected wounds*, after effective wound toilet, support is most conveniently provided by metal splints of the gutter or skeletal type, moulded plaster splints, or the complete plaster cast, padded or unpadded. Adequate support with its concomitant rest provides the optimum conditions for unimpeded healing of the wound, and brings nearer the day when movement can be substituted for inactivity. It should be remembered that the powerful reinforcement of modern chemotherapy, the sulphonamide drugs and penicillin, has not eliminated the necessity for rest and support of injured and infected structures in the early stages.

In *paralysis* of the lower neuron type—infantile paralysis and peripheral nerve injuries—the principle of support is exemplified in the use of the cock-up splint in the prevention of wrist-drop and the rectangular splint in the control of foot-drop.

Fixation—Here there is a sterner discipline, a combination of local rest, support and immobilization, designed to abolish movement, often for long periods of time—in the words of H. O. Thomas (1875) “enforced, uninterrupted, and prolonged rest.” Effective fixation is essential in the majority of *fractures* during the stage of repair, and periods of three to twelve weeks are generally necessary. Certain fractures, most notably fractures of the carpal scaphoid, may demand a longer period.

Much longer periods of strict immobilization are required in the treatment of *tuberculous disease of joints* when the diseased structures have to be protected from stress throughout the years which cover the stage of onset to the stage of quiescence and final repair.

In injuries and diseases of the *upper limb*, patients are usually able to lead an ambulatory existence, when efficiently and comfortably splinted. For immobilization of the shoulder there is the abduction (aeroplane) splint or plaster spica, for the elbow, the collar-and-cuff sling or plaster cast, for the upper arm, the plaster cast or gutter splints, for the wrist, the cock-up splint or plaster, and for the fingers, plaster or malleable metal splints which must be applied with precision.

In affections of the *trunk* and *lower limbs*, varying periods of recumbency may be needed in the earlier stages. Immobilization of the spine for fractures with neural complications calls for considerable technical resource if it is to be comfortable and safe. If an adequately padded plaster of Paris bed is used, highly skilled nursing must be available. In uncomplicated *fractures of the spine*, on the other hand, after correction of the deformity and wearing a complete plaster jacket, the patient can be made ambulatory in a short time and begin a graduated rehabilitation programme. In such cases, with the spine controlled in the position of hyperextension, fixation and protection are maintained until the healed fracture can safely take the stresses of unrestricted mobility.

In *Pott's disease* the formidable mechanical and nursing problems of immobilizing the spine over a prolonged period in a recumbent patient must be faced. Such patients also require the special regime suitable for the victims of tuberculous disease—open air, with controlled exposure to sun and wind, and a high quality diet. Various types of fixation apparatus are in use in the treatment of Pott's disease. The classical Thomas's frame, with special modifications, such as a sunken head piece for high dorsal disease, is widely used in orthopaedic hospitals in this country.

In the lower limbs the important rôle of traction, popularly known as extension, is illustrated by the immobilization of fractures and joint injuries, and in tuberculous arthritis or other destructive lesions of the hip and knee, in conjunction with various types of splint. In *tuberculous arthritis of the hip*, fixation with traction on the abduction frame provides effective mechanical control of the affected joint during the evolutionary stage of the disease. In the convalescent stage, fixation without traction is obtained by means of a plaster of Paris spica or moulded support of block leather or celluloid. In *tuberculous disease of the knee joint*, the Thomas bed knee splint, with traction in the early stages, the plaster of Paris cast at a later stage, and the weight-relieving caliper splint in the ambulatory stage, provide a sequence of events in the mechanical control of the diseased joint. The *tuberculous ankle joint* is effectively immobilized by a skeleton splint and later by a complete plaster of Paris cast with a walking heel.

In *lower limb fractures*, traction balanced by counter-traction with the limb cradled in a Thomas's splint is used in the fixation of fractures of the femur and some fractures of the lower leg bones. For many fractures of the tibia and fibula, ankle and foot, immediate fixation in a plaster of Paris cast and early weight bearing is the routine programme.

THE ILL-EFFECTS OF REST, SUPPORT AND FIXATION

It is well recognized that both general and local rest may be harmful when overprolonged or when enforced by too relentless immobilization. The long period of bodily inactivity and local immobilization necessary in the treatment of such affections as tuberculous disease of the spine or hip, tends to inculcate in the adult patient a state of boredom and to foster the loss of hope and courage. The child, on the other hand, suffers little, if at all, in this respect, and particularly when his education is provided for, as in the country hospital-schools. The full resources of diversional and occupational therapy are now regarded as an essential provision in hospitals for adult long-stay patients.

The physical and metabolic effects of prolonged inactivity have also to be reckoned with. It is well established that in the early days of destructive disease or after severe injury the patient suffers a rapid loss of tissue protein in excess of that due to simple non-use (Cuthbertson, 1937). In the majority of comparatively healthy individuals this loss is soon made up, but in prolonged disease a state of affairs may be established in which the protein content of the blood remains much below normal. This hypoproteinæmia is a factor antagonistic to the process of repair of the lesion and renders the patient more liable to develop pressure sores.

and bed sores. The risk of bed sores common to all patients who are immobilized, and particularly when elderly and frail, is obviously enhanced when various types of fixation apparatus are used. Frequent changes in position, again one of the features of the practice of the Hippocratic school, remains one of the essential precautionary measures of the nursing regime. A complication especial to prolonged immobilization in recumbency, occasionally seen in patients with Pott's disease or tuberculous disease of the hip joint, is the formation of kidney stones resulting from defective urinary drainage. This complication is almost unknown in patients who are regularly turned on to their faces, a manoeuvre which can be easily and safely carried out by means of a plaster of Paris turning case.

The harmful results of local rest are manifest in (1) disuse atrophy in muscle and bone, the latter being demonstrable in skiagrams as *osteoporosis*, a condition often erroneously referred to as decalcification but which is in fact a true resorption of bone without any change in its chemical composition, (2) stiffness of joints. These sequelæ are most marked and lasting in severe inflammatory diseases of the locomotor system—both non-suppurative and suppurative—and in lesions of the central and peripheral nervous system. It should be realized that they can either be completely prevented or their crippling effects minimized by the use of correct postures for the control of individual joints, and the purposive interpolation into the passive programme of rest—support—fixation, of active remedial measures at the earliest stage.

From the large-scale experience of organized rehabilitation in Ministry of Health and Service hospitals during the European phase of the war (1939-1945) it has been found that a suitable programme of activity can be prescribed with safety and advantage for all temporarily bed-fast patients who are not gravely ill. This applies to the sick as well as to the victims of accident. The latter have for many years reaped the benefits of rehabilitation measures in the organized orthopaedic-fracture departments which were one of the important features of hospital development in the period between the two wars.

The essential features of the active regime are that muscles passing over an immobilized joint should be contracted at frequent and regular intervals, and that a limb or joint not directly implicated should be put through a full range of movement daily. Not only is the physiotherapist introduced to the bedside during the regime of rest, but the occupational therapist also has an essential part to play in the selection of a diversion or craft suited to the needs of each individual patient. Thus, the physical measures of rehabilitation, or to use the new term, reablement, should be instituted at the earliest possible moment of the illness or injury. This harmonious blend of rest and movement is the outstanding characteristic of modern practice, for to-day support is given to the view of Hippocrates that "exercise strengthens and inactivity wastes."

References

- Cuthbertson, D. P. (1937) *J. Physiol.*, 89, 539.
 Hilton, J. (1863) "Rest and Pain," London.
 Thomas, H. O. (1875) "Diseases of the Hip, Knee, and Ankle Joints," Liverpool.

CONGENITAL DISLOCATION OF THE HIP

By GEORGE PERKINS, M.C., M.Ch., F.R.C.S.

Surgeon, St Nicholas and St Martin's Orthopaedic Hospital, Pyrford, Assistant Surgeon, St Thomas's Hospital

CONGENITAL deformities are of two kinds, in one of which the cause is faulty development and in the other an external force. The differentiation is of practical importance because, when development has been faulty, correction of deformity will not restore a normal anatomy, whereas restitution to the normal is possible in cases in which the structures are normally formed. Most cases of congenital dislocation of the hip belong to the latter group, for although the head of the femur is out of the socket, a socket exists suitable in size and shape for the reception of the head. At some time either just before, at, or soon after, birth the head is dislocated by an external force applied to the leg.

Although development proceeds along normal lines, the configuration of the bones forming the hip joint, in particular the head of the femur and the roof of the acetabulum, are modified in shape as a result of the unusual stresses associated with their unusual relative positions, and this divergence from the normal increases with time. Therefore the sooner the dislocation is reduced, the better.

There is, however, a more potent argument in favour of early reduction. Since the dislocated head and its surroundings accommodate themselves to their new positions, the longer the joint remains dislocated, the harder it is to uproot it and the greater the damage necessarily imposed during the process on all the structures forming the joint.

DIAGNOSIS

A prerequisite to early reduction is early diagnosis. The prognosis of a congenital dislocation of the hip depends more upon how early the hip is reduced than upon the skill of the reduction. The general practitioner, and not the surgeon, is the important person. It is unfortunate that museums and textbooks focus attention on disease in its ripe stages, and the fact that every museum specimen represents a medical failure is overlooked. The picture of congenital dislocation of the hip conjured up by skiagrams and preserved specimens of unreduced dislocations must be discarded. The diagnosis must be made, not in a woman of forty or in a girl of five, but in an infant who has not yet walked.

How is early diagnosis to be made? As the condition is painless, no help can be expected from the patient. An observant mother may notice that her child has an unusual shape and, indeed, in countries where congenital dislocation is endemic and therefore familiar, it is common for the mother to make the diagnosis herself. A British mother may be unaware that anything is the matter until the child is eighteen months old, then she becomes worried because the child has not learned to walk. Usually this brings the child to the notice of the general practitioner and he has an opportunity of establishing a diagnosis, but he will not succeed

in doing so unless he bears the possibility in mind. In cases of late walking, the general practitioner should always exclude a congenital dislocation of the hip. The diagnosis is not difficult to make if the hip is examined, but as it is not easy to examine in a routine manner the hip of a squalling, wriggling infant, the examination must be specific. Four signs should be looked for—(1) Female silhouette, (2) shortening of the leg; (3) diminished abduction in flexion of the hip, and (4) a hollow in Scarpa's triangle.

The female silhouette—The contour of a normal infant, whether boy or girl, resembles that of an adult male. When there is a congenital dislocation of the hip the pelvis appears widened, on account of the lateral displacement of the head of the femur, and the contour resembles that of an adult female. Often, also, the skin crease on the inner side of the thigh is higher than on the normal side.

Shortening of the leg—To measure with a tape is difficult because the child will not keep still. Shortening, however, can be shown by flexing the knees and hips until, with the feet flat on the bed, the femora are vertical, in this position, when there is shortening, one patella projects higher than the other.

Diminished abduction in flexion of the hip—If from the above position the two legs are abducted simultaneously, the loss of abduction on the dislocated side is obvious. Normally, 90 degrees of abduction is possible, so that the thigh touches the couch.

Hollow in Scarpa's triangle—In the flexed-abducted position the tendon of the abductor longus stands out, defining Scarpa's triangle, the floor of which is concave instead of plane. While the flexed-abducted position is being maintained by the examiner's elbows, the floor of Scarpa's triangle is palpated with the thumbs. As compared with the thumb on the sound side, the thumb on the dislocated side sinks into a hollow.

These four signs reveal clearly a unilateral dislocation. When the dislocation is bilateral, the diagnosis is more difficult because the skin creases on the thighs are level and there is no shortening, and the absence of a sound side makes it harder to demonstrate the loss of abduction and the hollow in Scarpa's triangle, the female silhouette is, however, more prominent.

X-ray findings—The diagnosis is tentative until confirmed by X-rays. The skiagram shows (1) that the roof of the acetabulum slopes upwards instead of being almost horizontal, (2) delay in the appearance of the bony centre of the epiphysis, which should be visible from about the third month onwards (if the epiphysis has appeared it is smaller than that on the sound side), and (3) displacement upwards and outwards of the shaft of the femur. This observation is rendered easier by the use of two lines, a horizontal line that runs from the centre of one acetabulum to the centre of the other, and a vertical line at right angles to the horizontal line and beginning at the outer extremity of the roof of the acetabulum. Normally the bony nucleus of the epiphysis is just below the horizontal line and just within the vertical line. If the nucleus has not yet appeared, the displacement of the shaft of the femur as regards the two lines is still to be made out. An experienced observer can diagnose a dislocation from the skiagram about one month after birth, diagnosis is not possible before this.

Whilst in general it may be said that a practitioner who does not diagnose a

congenital dislocation of the hip before the child begins to walk is incompetent, there are occasions when he does not see the child until after it has walked. The mother may then complain that the child limps, more often she has called in the family practitioner for some other minor ailment. The limp is a body limp and consists of a lateral inclination of the trunk towards the side of the dislocation when weight is being taken on that leg. It is readily spotted if attention is focused on the points of the shoulders. With a bilateral dislocation, the alternate dipping of the two shoulders gives rise to an unmistakable waddle gait. The gait may be mimicked by extreme bow legs. Not every limping child has a congenital dislocation of the hip, nevertheless, whenever a peculiarity of gait is noticed in a child a skiagram should be demanded by the practitioner with as much insistence as after an injury.

CHOICE OF TREATMENT

Although Dupuytren accurately described congenital dislocation of the hip over one hundred years ago, no treatment other than traction was attempted until about sixty years ago, when Hoffa introduced open reduction. He tenotomized all the resisting structures, including the muscles, and enlarged the acetabulum. Lorenz improved on Hoffa's technique and the method became known as the "Hoffa-Lorenz open method." This failed because most of the hips re-luxated and those that did not were either stiff or flail from the destruction of muscles. Then came Paci, who advocated closed reduction. He maintained that open reduction was unnecessary, since operation had shown that an acetabulum of fair size was nearly always present. Paci reduced the dislocation like a traumatic dislocation, but failed to prevent re-luxation. Lorenz, who had by now given up the open method, improved on Paci's technique and the method became known as the "Lorenz bloodless method." Lorenz showed that a more radical method of reduction was necessary and he spared the muscles, since he relied on them to hold the head in the acetabulum, and he pointed out the necessity of holding the hip abducted after reduction. Lately, the open method has come back into favour. Galloway, the prime advocate, advises that the operation should be done when the child is between two and two-and-a-half years old, without any previous attempt at closed reduction. Galloway from his operative experience declares that a narrow isthmus of the capsule is always present, and that in a successful closed reduction there is interposed between the head and the acetabulum a layer of capsule which is gradually worn away by attrition. Galloway regards the open method as simpler, safer and better than the closed method.

The controversy over closed versus open reduction is not yet settled. Many younger surgeons are in favour of the open method, although Putti, the greatest authority of all, preferred closed reduction. The prevalent British view may be summed up as follows —

- (1) After a certain age, attempts at reduction, open or closed, lead to so much stiffness and pain that the dislocation is better left untreated. Many unreduced dislocations are symptomless throughout life, and arthritis is more common in cases in which reduction has been tried and has failed than in those in which reduction has never been attempted. The age-limit

varies with the surgeon Putti puts the limit at four for bilateral and seven for unilateral dislocations, Fairbank at six for bilateral and nine for unilateral dislocations These figures all err on the liberal side It is to be hoped that with a greater awareness on the part of the general practitioner, and better facilities for X-ray examination, a congenital dislocation of the hip will in the future always be diagnosed before the age of three

- (2) Up to the age of twelve months, reduction can be achieved simply by holding the legs widely abducted
- (3) From the age of one up to the age-limit, closed reduction under anaesthesia should be attempted
- (4) If the hip cannot be reduced by a closed manipulation, the child should be returned to the ward and strong traction applied to the leg for a fortnight, after which another attempt at closed reduction should be made If that fails, open operation may be resorted to
- (5) If the surgeon does not feel satisfied at the time of the closed manipulation that the head has been reduced, and also if the skiagram taken afterwards does not show the head centrally placed in the acetabulum, open operation is indicated
- (6) Closed reduction is the method of choice

CLOSED REDUCTION

The hip should be reduced as soon as the diagnosis is made, because the earlier the attempt, the less the damage inflicted on the hip by the manipulation Treatment by closed reduction is divisible into three stages —(1) reduction, (2) fixation, and (3) convalescence

Reduction —The child is fully anaesthetized because muscle relaxation must be complete It is useless attempting reduction until the tight muscles have been stretched, i.e., until the trochanter descends to the normal level when traction is made on the limb and until full abduction in the flexed position is possible Often the hip reduces itself during the stretching of the abductors

Every surgeon has his own pet technique Denucé's method is as good as any —

A sandbag is placed under the pelvis to raise it off the operating table and an assistant fixes the pelvis by pressing down on the two iliac crests with the flat of his hands The thigh is flexed on to the trunk with the knee directed towards the opposite axilla In the case of a right-sided dislocation, the surgeon's right hand is placed on the knee and pressure is exerted in the direction of the thigh to force the head of the femur downwards The other hand is placed behind the great trochanter and, pressing in between the head of the femur and the wall of the pelvis, lifts the head forwards While this forward pressure is being exerted the thigh is circumducted across the body, outwards and downwards, into full abduction During the manœuvre the head can be felt to jump forwards into the socket

There is rarely any doubt about whether the hip has been reduced or not, the palpable shock is distinctive, the leg is no longer flail, the knee will not extend fully, and the head of the femur can be felt in the floor of Scarpa's triangle If doubt still exists the hip is re-dislocated and again reduced

After reduction the thigh is forced into further abduction until it lies in a plane behind that of the anterior superior spines, in order to stretch the anterior part of the capsule

If the hip has been truly reduced the thigh remains stable in the flexed-abducted position. The ease with which re-dislocation occurs is tested by moving the leg down towards the straight position and noting when the hip dislocates. The degree of stability influences the period of fixation.

Fixation—Fixation is required after reduction (1) to stabilize the head in the acetabulum and allow the capsule and the muscles time to accommodate themselves to their new lengths, and (2) to avoid pressure on the upper rim of the acetabulum until it has grown into a roof.

Plaster of Paris is usually used for fixation and the position of the hip depends upon the whim of the surgeon. The most popular position is that attained by flexing the hip 90° and then abducting it 90° . The hip is held in plaster for about a year. Some surgeons maintain the same position throughout, others gradually reduce the amount of flexion and abduction.

After the anæsthetic the child is usually incontinent until he has been re-trained and to prevent the soiling of the plaster the edges are lined with mackintosh sheeting and the child is nursed mostly on the face, with a urinal always in position. As soon as the mother has learnt how to prevent the plaster from becoming soiled she may take the child home until the plaster is due for renewal in three months' time. Anæsthesia is needed to change a plaster, and the surgeon must satisfy himself after every change of plaster that the head remains truly reduced. It is futile to leave the hip in plaster unless a central reduction has been obtained.

Convalescence—After the plaster is finally removed the child is left free to kick about in bed. Suspending the child in a bath full of water, as though teaching him to swim, is excellent. The child is not encouraged to stand, but is not checked when beginning to do so. During this period the child should be in hospital so that the hip can be inspected frequently and appropriate steps taken should re-dislocation threaten.

RESULTS OF CLOSED REDUCTION

Definitive results can only be judged after the lapse of many years. Even when the treatment has been directed throughout by an expert, only half the cases can be classified as good.

Not uncommonly after a successful reduction at which little force was used the head of the femur undergoes the changes of *pseudocoxalgia*. This is presumably the sequel to an injury to the blood supply of the epiphysis.

Limitation of range of movement—Occasionally the hip joint becomes painful and its range of movement limited by muscle spasm. This may happen soon after the plaster is removed or may be delayed for a year or so. The cause in either case is unknown. Later in life the joint may wear out prematurely and show signs of osteoarthritis, as is usual whenever the surfaces of the acetabulum and the head of the femur are incongruous.

Re-dislocation—An X-ray should always be taken on the removal of a plaster and after the application of a fresh plaster. At any time during the period of fixation the skiagram may show that the head has re-dislocated. Most early re-dislocations are cases in which the head has never been truly reduced. After a central reduction,

re-dislocation during the period of fixation does not happen unless the plaster has been loosely applied or unless the hip has been held in a faulty position. Re-dislocation may not take place until some time after the hip has been freed from plaster. Late re-dislocation is almost invariably due to lack of development of the roof of the acetabulum. Should it happen, the hip is again reduced and a roof constructed at an open operation.

Anterior transposition—Sometimes the original posterior dislocation is changed into an anterior reposition and the head of the femur comes to lie in front beneath the anterior superior spine. Anterior transposition may happen spontaneously (a) at the time of reduction, or (b) during the period of fixation in plaster, or (c) after the hip has been freed from plaster. It may also be brought about intentionally. Transposition in lieu of true reduction ought not to escape the observation of the surgeon. It is a matter of dispute whether anterior transposition, which is often feasible when reduction is not, is better than the original posterior dislocation. It is advantageous in that it gets rid of the ugly lordosis and renders the dipping gait less noticeable, but there is a tendency to regard it as little worse than a true reduction, which is a fallacy. Transposition occurring during fixation in plaster is common, and as soon as it is recognized the plaster should be removed and reapplied, after the leg has been rotated in. Transposition occurring after the hip is freed from plaster is also common and is due to excessive antversion of the neck of the femur. After coming out of plaster the hip should be inspected frequently, and if the head becomes prominent in Scarpa's triangle the amount of antversion is estimated under the X-rays and neutralized by osteoclasing the shaft of the femur and rotating the lower fragment out.

OPEN REDUCTION

Open reduction is the method of choice when there is (1) an anatomical obstacle to reduction, (2) a late re-dislocation, and (3) marginal displacement.

Anatomical obstacle to reduction—Failure to reduce should not be assumed to be caused by an anatomical obstacle until reduction has failed a second time after a period of traction on the leg.

The obstacle is either extracapsular, and due to the adherence of the capsule to the side wall of the pelvis above and behind the acetabulum, which prevents the downward excursion of the head, or intracapsular, and due either to an hour-glass constriction of the capsule or to too small an acetabulum.

Late re-dislocation—In spite of a true reduction and proper fixation, the hip may re-dislocate after the removal of the plaster, owing to the absence of an adequate roof to the acetabulum. It should be noted that the X-ray is not an infallible guide to the state of the acetabular roof. The roof may be adequate but invisible, because unossified. Often when the hip is freed from plaster the skiagram shows a sloping roof which in the course of years becomes horizontal. Progress should therefore be followed by serial skiagrams taken at three-monthly intervals. If the head remains on a level with the head on the normal side, all is well. If the skiagrams show that the head is slowly rising, re-dislocation is inevitable and should be forestalled by an operation at which a new roof is constructed.

Marginal displacement —The original skiagram may show that the head, although in the acetabulum, is slightly up and out. This indicates the complete absence of a roof. In such cases Fairbank says it is useless to rely on closed reduction for, although the head can be easily replaced in the centre of the acetabulum, relapse is certain. The acetabulum never becomes a cup but remains a saucer, and a subluxation persists throughout life. A subluxated hip causes more trouble later in life than an actual dislocation, and accordingly Fairbank advises that in cases of marginal displacement the hip should be operated upon without delay and a roof constructed.

TYPES OF OPERATION

(1) *Extracapsular open reduction* —This is indicated when two attempts at closed reduction have proved the presence of an anatomical obstacle.

The hip is approached by the Smith-Petersen method. With the aid of a chisel the capsule is stripped off the ilium above and behind the head. The capsule is not opened. When sufficient capsule has been freed to allow the head to descend to the proper level the head is "shoehorned" into the acetabulum.

(2) *Intracapsular open reduction* —If after the capsule has been freed reduction is not possible, the capsule is opened and the crescentic fold of synovial membrane which projects from the upper posterior margin of the true acetabulum and acts as a barrier to reduction is divided. If reduction is still unsuccessful by reason of the smallness of the socket, the acetabulum is cleared of its soft structures, the ligamentum teres being preserved if possible. Enlarging the socket by curetting away cartilage and bone should not be done, as this leads inevitably to a stiff hip.

(3) *Formation of a roof to the acetabulum* —This may be the sole object of the operation and is indicated when late re-dislocation has occurred and in cases of marginal displacement. A roof should also be formed whenever the hip is operated upon, even when the prime object of the operation has been reduction. The capsule must first be freed from the side wall of the ilium, and one of the difficulties of the operation is to continue this freeing low enough. Unless the capsule can be freed as far down as the edge of the true acetabulum the new roof will be constructed too high. The other important point of the operation is to make the roof wide enough.

A curved osteoperiosteal flap is turned down from the side of the ilium, one-third of an inch above the upper margin of the true acetabulum and held horizontal by a wedge of bone obtained from the crest of the ilium. This is hammered into the cleft between the ilium and the flap. The graft usually stays in position of its own accord, nevertheless, it is as well to secure it with one or two small bone pegs. Afterwards a plaster is applied holding the hip in the position that was found at the time of the operation best to centralize the head in the acetabulum. This position is held for three months.

CONGENITAL DISLOCATION OVER THE AGE-LIMIT

Reduction should not be attempted over the age-limit because, even if the reduction is successful, the invariable result is a stiff painful hip. Many patients with unreduced congenital dislocations of the hip pass the whole of their life without seeking medical advice about their hip. Those with symptoms complain of

(1) shortening of the leg, (2) unsightly lordosis, (3) dipping gait, (4) pain due to deformity of the hip, and (5) pain due to arthritis of the false joint

Shortening—Shortening can be compensated for by a raised shoe, but the limp due more to the dipping gait than to the shortening, and the raising of the shoe defeats its own object by making the patient conspicuous. Women, in particular, dislike not being able to wear ordinary shoes

Unsightly lordosis—This is caused partly by the downward tilt of the front of the pelvis and partly by the swaying back of the trunk in an endeavour to bring the body weight over the backwardly displaced femur. The lordosis is much increased if the hip develops a flexion deformity. An ugly lordosis often warrants treatment. In young children some surgeons favour anterior transposition, i.e., converting the posterior dislocation into an anterior. Others advocate osteotomy of the femur for young, as well as for older, children

Dipping gait—Two procedures are in vogue—(a) turning down a flap of ilium over the displaced head, and (b) osteotomy. Osteotomy is simpler and, as it gives as good a result, is preferable. It diminishes lordosis and abolishes pain due to deformity of the hip and largely gets rid of the dipping gait.

Pain due to deformity of the hip—There may be pain in the back on account of excessive lordosis, and there may also be a pain in the hip from stretching of the capsule. Osteotomy can be relied upon to cure both pains

Pain due to arthritis of the false joint—Before deciding on treatment for pain, it must be determined whether the pain in the hip is due to the hip deformity or to arthritis. If due to deformity, the pain is felt on weight bearing and there is no pain when the leg is moved on the couch, also the range of movement is wide. If due to arthritis, pain is felt on movement, the range of movement is narrow and the hip is held flexed and adducted

For pain due to arthritis, the only cure is an arthrodesis, but a sound ankylosis is not always easy to obtain

CONGENITAL SUBLUXATION OF THE HIP

Normally the half-spherical head of the femur fits into the half-spherical cup of the acetabulum. Sometimes, however, the acetabulum is saucer-shaped instead of cup-shaped, and the head of the femur rises in the acetabulum during weight bearing. According to Putti, subluxation of the hip is more common than true dislocation, and in later life causes more trouble than an unreduced dislocation. There are no symptoms in children and the subluxation cannot be diagnosed on clinical examination. The skiagram, however, shows that the head of the femur, although in the acetabulum, is further up and further out than it should be

Putti was in favour of treating a subluxation in exactly the same way as a frank dislocation and of fixing the hip in abduction for the same length of time. Fairbank believes that every patient with a subluxation should be operated upon and given a new roof to his acetabulum.

MALUNION OF FRACTURES

BY R. BROOMHEAD, F.R.C.S.

Orthopaedic Surgeon, General Infirmary, Leeds, Lecturer in Orthopaedics, University of Leeds

IN this article it is proposed to discuss one of the failures of medicine—malunion of fractures. It is rather surprising to find that at this period of fracture history "malunion" should be regarded as being frequent enough to be discussed in an important journal. Recently, it had seemed that all was right in the fracture world: apposition and alignment perfect, union complete and rapid, the slightest loss of function almost an unknown quantity—that, in fact, the paradise of insurance companies had been reached.

Those working in an up-to-date fracture clinic attached to a teaching centre are apt to regard malunion as a rare occurrence. However, the request to write an account of "malunion," and the appearance of one or two recent cases have rather shaken an impression of tranquillity, as the following example will show —

A few weeks ago I was asked to see a patient, a woman in the late twenties, married with a husband abroad. She had been knocked down accidentally, but through her own fault, in October 1944. She was treated at a small hospital by a general practitioner-surgeon. She had a fracture of the lower third of the right humerus, which was treated by putting the arm into plaster. The patient was told that the position was good. In January 1945, when the plaster was removed, she was told that the bones had not united properly, and that they would have to be plated! This was done and, as the surgeon naively wrote afterwards, "while the humerus was being cleared, the musculo-spiral nerve was cut, but it was immediately sutured." The operation wound was infected and was discharging when I saw her in March 1945. She had a septic open fracture plus a complete musculo-spiral palsy with a range of about 30° movement at the elbow.

It may be said with some truth that this is not a pure example of malunion. Perhaps not, but the technique is such and the standard of treatment so appalling that it is possibly the justification in 1945 for an article on malunion.

To discuss malunion completely, prevention, as well as treatment, must be considered, but to deal efficiently with prevention would necessitate a review of the early treatment of almost all fractures. This article is not intended to be a treatise on the treatment of fractures, and it will therefore be confined to dealing with established malunion in its various and common sites, pointing out how in the particular fracture in question, prevention could have replaced the cure.

In this article the definition that "malunion is union in such a position as to interfere with function" will be adopted. Function may be interfered with because of a bony block to movement, because bony deformity causes interference with the movement or weight bearing of nearby joints, because of the direct involvement of a joint, or because pain is present.

TYPES OF MALUNION

There are certain sites, for example, the forearm, where union is often in such a position that the normal range of movement does not return, but function itself is relatively unimpaired because the loss of rotation is compensated by movement at the shoulder joint, and no further treatment is possible or even necessary. Such cases are not considered here.

There are some sites where malunion is often the rule rather than the exception, in spite of what is done even in the best clinics, for example, fractures of the os calcis and other tarsal bones, and fractures into joints with disturbance of the articular surfaces.

There is still a third group in which malunion should not occur, but in which it is encountered with a depressing regularity—when it has become one of the failures of surgical treatment. Therefore, by and large, malunion should not occur; and perhaps the most important thing that can be said about its treatment is that in the majority of cases the establishment of malunion is preventable, and that when it occurs it reflects a most unfavourable light upon the way in which the fracture has been treated.

As this article is not part of a treatise on orthopædics, but presumably is meant for general practitioners, who by desire or force of circumstances have to treat fractures, it is unnecessary to describe methods of treatment used for cases which, because of their severity, will almost inevitably result in some degree of malunion, and which should be transferred to an up-to-date fracture clinic where there are full facilities for all the mechanical ingenuity that fracture surgeons now display. Instead, it is proposed to describe the points to be observed so that malunion does not occur in the "preventable" cases.

In most cases loss of function is due to faulty alignment. It cannot be over-emphasized that of the two features to be observed in deciding whether the skiagram of a treated fracture shows a satisfactory result—alignment and apposition—alignment is by far the more important. If the two main fragments of bone in a fractured limb are not in alignment, malunion is a fair certainty. Likewise, if the main fragments are rotated, malunion is probable. If lateral displacement is bad, and especially if the fracture is near a joint, or where the bones really form part of a joint, as in the forearm, malunion will result. Again, fragments of bone that project near joints may lead to malunion by virtue of their mechanical interference with joint movement. Malunion may also result if the limb is not efficiently splinted when bed immobilization ceases, for example when there is a low fracture of the neck of the femur. These examples are mostly in the lower limb and are the result of unrestricted weight bearing.

CLASSIFICATION

There are certain lesions in which malunion is common, and is often unpreventable—

- (1) Fractures of the os calcis, and other tarsal and metatarsal bones
- (2) Communited fractures into joints

- (3) Severe compound fractures, particularly those sustained in warfare.
- (4) Fractures of the radius and ulna.

There are other fractures in which malunion is common, but is preventable. The cases which come into this group are due either to the patient being away from adequate medical care, or to ignorance or neglect on the part of the medical practitioner, be he general or special.

Examples in this group are —

- (1) Fractures of the tibia and fibula and shaft of the femur
- (2) Low fractures of the neck of the femur
- (3) Supracondylar fractures of the humerus
- (4) Fractures of the metacarpals and phalanges of the fingers

TREATMENT

Treatment depends upon how late the patient is seen after the accident. In some fractures of long bones, for example, Colles's fractures or fractures of the tibia and fibula, it may be possible within a few weeks after the accident when apposition is not satisfactory or when there is an angular deformity, to correct the error by simple leverage or by wrenching with a Thomas's wrench. Adequate immobilization will then prevent malunion. On the other hand, when solid bony union is established the problem is far more difficult.

Treatment of established malunion — Since there is a tendency at the present time to devise more and more elaborate operations, it may perhaps be as well to stress that much can be done by relatively simple methods for patients with malunion, and it must be borne in mind that the aim is to improve function, not a skiagram. It is no great surgical triumph to produce a skiagram with correct alignment if function is no whit better. There is nothing more fallacious than X-ray diagnosis and treatment.

If a patient has a malunited fracture his loss of function is often due to loss of movement, but that loss of movement is not certain to be due to bony causes. Loss of movement is often due to adhesions of soft parts which can be broken down and mobilized by careful, and possibly repeated, manipulations under anaesthesia. If such procedures are interspersed with periods of concentrated physiotherapy, although there may not be a full return of normal function, it may be possible to restore enough movement to give the patient adequate function, and major operations may be evaded. This is particularly so when the fracture has been in the region of a joint.

DETAILS OF TREATMENT OF MALUNITED FRACTURES

As this article is primarily for practitioners and not for fracture specialists, it is proposed to deal first with the lesions of apparently lesser magnitude which are likely to be treated as ambulatory cases, and which are not regarded as sufficiently serious to send to a fracture surgeon.

Phalanges of fingers and metacarpals — Malunion in these cases is due to rotation or angulation at the site of fracture, or to a fracture into a joint where healing has occurred with a bony projection containing part of the joint surface. Angulation and rotation can easily be prevented if it is remembered that the adjacent finger is the best splint. If two fingers are bandaged together, the deformities of angulation and rotation which lead to much impairment of range and power of grip will be prevented. If a bony spur is present and is preventing movement it should be removed, so long as its removal will not leave an unstable joint. Fingers, however, respond so well to manipulative treatment that major procedures should always be carefully weighed in the balance against something relatively simple. Careful manipulations, possibly repeated on one or more occasions, will often effect marked improvement in function in these cases. In fracture and orthopædic treatment, always remember the bonesetter!

Colles's fractures — Malunion in these fractures is still depressingly common. Good function is the rule in a well-organized fracture clinic, but in the country and at the cottage type of hospital it is surprising how many patients have a radially adducted or backwardly displaced lower fragment, together with loss of forearm rotation and loss of power of grasp. These malunions are often associated with a good deal of pain. When there is incomplete reduction of two or three weeks' standing, it is occasionally possible to correct the deformity and prevent malunion developing by breaking down the fracture with a Thomas's wrench. After reduction of the fracture, the forearm can be fixed in plaster for six weeks or so, with good effect. Manipulation may help some of them; others are best left alone, if function be moderately good, but, if treatment be imperative, a wedge-shaped osteotomy to correct the deformity of the radius, followed by fixation in plaster for eight weeks, will give marked improvement. Occasionally a projecting bony spur may be removed with advantage.

Radius and ulna — When these two bones are malunioned it is probably wise to leave them alone so long as the loss of forearm rotation is compensated by rotation at the shoulder. If the bones are badly angulated, linear osteotomies of both bones at the sites of deformity, followed by prolonged immobilization in plaster, will effect an improvement.

The humerus — Supracondylar fracture. Malunion here is usually due to angulation causing cubitus valgus or varus. If an angular deformity is discovered two to four weeks after the fracture has occurred, it is wiser to wait until bony union is complete and the child has recovered full range of movement, before trying to correct the deformity. Operative attempts to correct the condition during these weeks usually result in marked stiffness of the elbow. If, on the other hand, the child has been allowed to regain a fully mobile elbow, the deformity can be corrected by taking a narrow wedge of bone from the supracondylar region of the humerus. The limb is afterwards fixed in plaster for six weeks, with the elbow in extension and the deformity corrected. Remedial treatment will then restore full movement.

Shaft and upper end. Angulation of the shaft may occasionally cause trouble and may require a corrective osteotomy, but more often there is malposition at the upper end, due either to a separated epiphysis, to a fractured surgical neck,

or to a fracture-dislocation of the shoulder complicated by a fracture of the greater tuberosity which causes trouble by projecting as a bony lump

Experience with these cases is that bony deformity alone does not cause much trouble. Loss of function is due to adhesions between soft tissues and is usually best improved by manipulation under anæsthesia

Metatarsals—Malunion often depends upon the degree of displacement at the time of the accident. It can usually be avoided if the foot is carefully moulded and put into plaster at the time of the injury, and again when swelling has gone. If loss of function develops, much can be done by remedial and manipulative treatment to free the foot and make it mobile. If there is bony deformity, removal of a spur may be helpful

For bad cases, if it is thought that function can be improved, I have devised an operation, some results of which I showed to the British Orthopædic Association on its visit to Leeds in May 1944, and which I called "reversal," or perhaps more properly "rotation," of the metatarsal. The offending metatarsal is exposed and its periosteum separated from the shaft so that the bone lies free. The metatarsal is divided about half-an-inch from the base, and the capsule around the head is freed so that the bone can be removed. Any projecting spurs are removed and the bone is then replaced so that its cut surfaces are in contact, but it is rotated so that the upper surface is now underneath and the under surface on top. The foot is then carefully moulded and put into plaster for two or three months. The operation is not difficult, but it demands a sound surgical technique

Toes—When malunion follows fractures of the toe phalanges, it is best dealt with by arthrodesing the toe joints so that they are ankylosed in the straight position

Tarsal bones—The bones particularly concerned are the os calcis and the astragalus. To give the best result, a malunited astragalus may require an extensive arthrodesis of the foot

The last word does not appear to have been said about the treatment of fractures of the os calcis. When malunion is present and is giving rise to pain, a subastragaloid or a triple arthrodesis may be the method of choice. Manipulation offers no hope

Fracture-dislocation of the ankle—This injury still gives rise to a depressing number of "limpers." Bad function is due to non-reduction. The foot usually remains displaced outwards, although occasionally backward displacement of the astragalus remains uncorrected. There is no reason why these fractures should not be adequately reduced. Even in cases of non-reduction, function is often moderately good for a number of years until osteoarthritis of the ankle causes the patient to seek further treatment. When osteoarthritis is present, arthrodesis of the ankle is the best method of treatment. In those cases seen early with loss of function and deformity, Jones's operation gives good results. The operation consists of the removal of a wedge from the supramalleolar part of the tibia, plus an osteotomy of the fibula, after which, the deformity is corrected. The gap which is thus created at the fibular osteotomy is filled with bone taken from the tibia.

Tibia and fibula—The common deformities here are internal and backward angulation, although some degree of internal rotation deformity is frequently seen. Important shortening after these fractures is so rare as to require only passing mention

Angulation and rotation can be prevented if full reduction and immobilization are practised. When deformity is present, correction is attained by osteotomies, followed by moulding and plaster until union has occurred. When union is not absolute, deformity can be corrected by levering the limb into proper alignment under anæsthesia.

Fractures involving the knee joint—In these cases, whether the tibia or the femur has been broken, little need be done unless the patient has developed a painful osteoarthritis, when arthrodesis of the knee may be preferred to a knee cage or walking caliper.

Fractures of the shaft of the femur—Here again loss of function may be due to backward angulation caused by inefficient support behind the fracture. When it gives rise to a badly functioning "back-knee" or genu recurvatum, an osteotomy, followed by correction of the deformity and adequate fixation until union has occurred, will give marked improvement, although it must be borne in mind that two periods of fixation will inevitably give rise to a stiff knee.

Loss of function sometimes results from outward bowing in upper- and middle-third shaft fractures. Bowing is usually due to inadequate traction, and when fully developed is difficult to correct and maintain corrected, as there is a marked tendency for the deformity to recur. If loss of function is serious, an osteotomy at the site of fracture, followed by strong skeletal traction and prolonged immobilization, will correct most of the deformity, although the resulting loss of knee movement may be an equally embarrassing condition.

Shortening after fracture of the femoral shaft is not a common cause of loss of function. It can be prevented by carefully guarding the fracture during weight bearing. It is important to stress the fact that shortening accompanies many low fractures of the neck and trans-trochanteric fractures, because the weight-bearing splint is discarded too soon.

Compound or open fractures—In certain of these fractures, particularly those caused by modern warfare, malunion may be the only possible result, particularly when to obtain union at all may be considered a therapeutic triumph. In such cases no reproach attaches to the surgeon, but the inevitability must be faced and be put frankly before the patient or his relatives.

Fractures of the spine—Spinal malunion occurs when marked wedging of the damaged vertebræ remains. When malunion is present, function can often be improved by manipulation, whereas if this fails, fusion may give relief.

AMPUTATION

Nothing has been said about amputation—that confession of failure—but there are certain cases of malunion in the feet and fingers when loss of function is such that amputation will result in improved digital and ambulatory function, and it should therefore be considered as a method of treatment.

SCIATICA AS AN ORTHOPÆDIC PROBLEM

By KENNETH H PRIDIE, F R C S

Surgeon to the Fracture Department, Bristol Royal Hospital

THE association of sciatic pain with lesions of the intervertebral discs was discovered in 1934. Its importance as a cause of sciatica and backache is not yet fully appreciated. The story of such an association was brought to this country from America by J Barr in 1938, when he spoke at a B M A meeting at Plymouth, where I was one of the unbelievers on whose ears the truth fell with little impression. Until this date I was well satisfied with the results of the treatment then in vogue for patients with chronic sciatica, which seemed to cure them. Why then was this new conception of a lesion advocated? Were not the upholders of the new views going too far? Surely a ruptured disc must be a rare lesion, so why worry when the old treatment was so successful?

THE OLD CONCEPT AND TREATMENT OF SCIATICA

What was the old treatment? The acute sciaticas were all seen by the physician and did not come the way of the orthopædic surgeon. Besides, no orthopædist would be interested in anything but a chronic sciatica of six months' duration or more.

The opinion of physicians was that 90 per cent of sciatic pains were of rheumatic origin—a delightfully vague and non-committal phrase which covered most pains about which little was known. Further, they thought that cases which became chronic were due to peri-neural fibrosis as a result of the prolonged inflammation of the nerve. If the case could not be attributed to rheumatism it was thought to be probably due to lack of vitamin B—a kind of beri-beri.

The treatment depended upon which day the patient entered the out-patient department. If on a Monday and seen by the physician he was put to bed for six weeks, lying absolutely flat. If on a Tuesday, under the orthopædist he was treated for weeks in a plaster cast, and if on a Wednesday and the neurologist was on duty he might have an epidural injection of saline, magnesium sulphate and novocain into the sacral canal.

The line of treatment I found most successful was a manipulation under anaesthesia together with an epidural injection, great stress being laid on the stretching of the sciatic nerve. If this did not cure the patient or improve his pain the sciatic nerve was exposed and stretched. This was a most successful operation and rarely failed to relieve the patient. Many fibrous bands appeared to be present around the sciatic notch and the nerve was freed and well stretched. Stretching the sciatic nerve after exposure has been used almost since the days of Lister, but it is difficult to see why it relieves the patient. Perhaps the pain fibres are thereby destroyed.

When a surgeon is pleased with his results it is difficult for him to accept any new treatment, in fact, he resents new ideas which, to say the least, are a bit disturbing.

THE NEW CONCEPT AND TREATMENT

I returned from Plymouth determined to try this new treatment, and the next two cases of sciatica of traumatic origin of more than two years' duration were investigated by lipiodol and a filling defect was found. A laminectomy was performed in both cases.

The first, a negro, showed a good filling defect between L 4 and 5 on the right side. At operation a complete laminectomy was performed, three spinous processes were removed but no disc was found. However, the patient's sciatica was relieved and he was most grateful. Although he still has a slightly unstable back he served through the whole of the "blitz" in the Air Raid Rescue Squad.

The second case was a policeman who had what appeared to be a typical disc lesion. A lipiodol injection showed a filling defect. At operation a full laminectomy was performed, and in this case such formidable bleeding was experienced that finding a disc was out of the question and the wound was closed. The next day the patient firmly declared that the pain had gone. He returned to full duty and has been seen six years later with another complaint—a ruptured biceps femoris muscle—and he has no complaint to make about his back or leg.

These results were most puzzling, for the cause of the sciatic pain was still unexplained. Whatever the treatment, the patient appeared to improve. Was the condition one of neurosis?

At this time further protagonists came from the States in the form of American Army medical officers. Nothing could shake their faith—they knew all about it, and what is more they knew how to remove these discs. My complete conversion to the theory that the disc can and does cause sciatica, and is by far the most common cause of chronic sciatica, was brought about by Dr E Kahn. The case was a typical one—

A man aged thirty-five was lifting a heavy weight when he felt something go in his back. He thought he had been shot in the back as the pain was excruciating and he was unable to move. He stayed in bed for six weeks and so great was the pain in his leg that morphine had to be given after the acute stage had passed. He was never free from pain but was able to walk about and do light work. On examination it was obvious that the sciatica in the right leg was connected with a lesion of the back, for he had a contra-lateral scoliosis, a lumbar kyphosis, a lost ankle jerk and altered sensation over the outer side of the leg. X-rays showed a diminished disc space between the 5th lumbar and 1st sacral vertebrae. The disc was demonstrated by myelography, and later at operation a sequestered disc was found and removed. No bone was removed, the whole exposure being through the ligamentum subflavum.

Since this case I have followed up all my old so-called sciatica cures and find that they have had relapses and wandered from practitioner to practitioner in search of a cure.

One patient with severe sciatica, after exposure and stretching of the nerve, returned with a recurrence after working as a farm labourer for six years, during which time he had been completely free from pain. When seen in 1945 he had typical disc signs—severe sciatica of over three months' duration, lost ankle jerk, contra-lateral scoliosis, loss of disc space as shown by the lateral X-ray, and pain radiating down the sciatic nerve on coughing and sneezing. He also had tenderness, and aggravation of the sciatica when pressure was applied over the ligamentum subflavum between the 5th lumbar and 1st sacral vertebrae. At operation the patient was found to have a sequestered disc, i.e., a prolapsed disc free in the spinal canal.

On reviewing this case it is seen that the original condition for which the operation of neurolysis was performed was really due to a ruptured intervertebral disc. Why then did the operation of neurolysis relieve the symptoms? The answer

must be that, on freeing the nerve, the nerve root is less taut over the ruptured disc, and therefore the nerve pressure and symptoms are relieved. I was able to confirm this by performing an experiment in the post-mortem room. I exposed and pulled upon the sciatic nerve (in the thigh) and then performed a total laminectomy, and saw the amount of play in the nerve root that was produced by this operation. While stretching the sciatic nerve in the back of the thigh distinct movement could be seen in the nerve roots as they left the dura in the lower lumbar region. If therefore a disc were present after the stretching of the nerve, the nerve root might be freed from the disc and take up a position either medial or lateral to the protrusion. This would probably account for the dramatic relief of pain following manipulative treatment or stretching and neurolysis of the sciatic nerve.

A word of warning, however, must be given concerning the treatment of disc lesion by manipulation under an anæsthetic.

I happened to hear of a case of chronic sciatica that had been treated for years as hysteria and was subsequently manipulated. On vigorous hyperextension something was felt to crunch in the back. The next day the patient had paralysis of the bladder, a saddle-shape area of anæsthesia around the anus, and foot-drop, with weakness of the gastrocnemii. At a subsequent operation the disc was found to be completely sequestered.

It would therefore seem that it is most dangerous to use vigorous hyperextension when manipulating a case of chronic sciatica or backache.

The attitude of the medical practitioners of this country to this new concept of sciatica is rightly somewhat cynical, as is shown by the following correspondence in a case of sciatica —

"Dear Dr

This chap is alleged to have that extremely useful and modern invention—a prolapsed intervertebral disc. He got out of the Army on the strength of it. He was under you in 1940 and was treated by manipulations. Two years later he was admitted under a physician and treated by rest in bed. His constant complaint is pain in the right leg, which according to him is of a most crippling character. He is an extremely neurotic young man and, personally, I think he is going to give a lot of trouble. I would be grateful for your views on treatment.

Yours "

I examined this patient and to me he had a typical ruptured intervertebral disc in that he had sciatic pain with a lost ankle jerk, and symptoms of nerve pressure on the 1st sacral nerve. This was associated with a back lesion, as he had a deviation of the spine away from the painful side and a lost lumbar curve. It seemed obvious that the cause of the trouble was in the back and pain was referred down the 1st sacral nerve root. I therefore wrote to his family practitioner saying that I considered that the man had a ruptured intervertebral disc, the case was true to type, and that I would be glad if he would attend the operation when he would either be converted to the new theory or else disillusioned. I also pointed out that it was impossible to argue about the disc unless one had been converted.

The practitioner wrote back, saying —

"Thank you for your homely re Mr X and his ruptured intervertebral disc. Mr — who was not the biggest fool that ever graced the Infirmary staff, once remarked to me 'that he prided himself that he remained two years behind the fashions'—this was after viewing three cases in a ward, all of whose fractured tibiae had been plated by an enthusiastic still a colleague of yours, and all of whom had suffered amputations as the final result. You can take it from me that removing intervertebral discs is very much in the fashion at the moment, and I sincerely hope that history will justify all these operations, but I am not convinced of it yet.

Yours

P S—I would very much like to see a disc removed, without prejudice, of course "

This patient was very fat and great difficulty was experienced in removing the disc. However, it was a true bill. The nerve root was adherent to the disc and the disc was removed. The patient made a good recovery, the only complication being an infected hæmatoma in the back, but this cleared up and the patient was very satisfied with his condition, completely losing his sciatic pain.

INDICATIONS FOR OPERATION

The great danger with this new concept of sciatica is that many unnecessary operations will be performed. It is not an operation that should be lightly undertaken, nor has it been performed for sufficiently long to show the absolute end-results. There are certain questions that will have to be answered.—

- (1) How long should a case of pain in the back associated with pain distribution along the lumbar nerve roots be given conservative treatment before operative measures are resorted to? Is it right to wait until there is such evidence of nerve pressure on the root that the ankle jerk is lost? Once the ankle jerk has been lost it may never be recovered, even though the nerve root pressure is relieved. Is it right to wait until there is nerve damage or should the patient be operated on when there is evidence of nerve irritation?

- (2) Is the patient able to do hard manual work after the removal of a disc?

It seems that there is a double problem. The patient first has an unstable back which leads to a ruptured intervertebral disc. While the disc is degenerating he gets attacks of lumbago which may be a yearly occurrence and which settle down with rest. In this state the disc is degenerating and altering in its consistency. When the disc starts travelling backwards through the annulus fibrosus and protrudes into the spinal canal the patient gets acute attacks of pain. The disc protrusions are generally lateral but they may be central. If they are central they are sometimes not associated with sciatica but may cause some difficulty in micturition. If the protrusion is lateral it will impinge on the nerve roots as they travel outwards to the neural notch. So often at operation the nerve root is found to be adherent to the disc lesion, and it is only with the greatest difficulty that it can be separated from the protrusion. This explains the presence of a filling defect in the myelogram, as a small pouch of the dura comes down on the nerve root for a considerable distance and the lipiodol can travel down this, casting a well-marked shadow. A filling defect of a nerve root then would indicate that there is pressure from below obliterating the lateral dural diverticulum. If the patient does hard manual labour at this stage he may get a sudden onset of acute sciatica sometimes the pain is excruciating and is not even relieved by morphine. This suggests a complete extrusion of the disc. In 20 per cent. of the cases I have operated on I have found a completely sequestered disc.

POST-OPERATIVE RESULTS

When the disc has been removed the spine is still by no means normal and there is still the problem of the unstable back. Even following operative removal of the offending disc the patient may still have some symptoms, and in consequence

the operation may be liable to come into disrepute, since the patient is not completely cured. The practice of the American Army with regard to this seems to be that any soldier with a diagnosis of a ruptured disc should not be operated on in the Army but should be sent back to America for the operation, as it is considered that he will be unfit for the Army, since he is still left with an unstable back on account of the double pathological condition, viz, the ruptured intervertebral disc and an unstable back, and a nerve pressure syndrome.

By operation the pressure on the nerve can be removed but some patients will need a second operation for stabilizing the back, by a graft between the two affected vertebræ. It has been my policy in these cases to relieve the nerve pressure first, by damaging as little bone as possible whilst approaching the disc to remove it. In 80 per cent of the cases no bone at all need be removed. After the operation all patients voluntarily give the information that their sciatica is completely cured. If, however, they find they have an unstable back which persists and they are not able to follow their normal work, a bone-grafting operation will have to be considered. In the past a number of these cases must have been treated by fusion alone. This sometimes produces a cure but it gives a big additional complication to any further operation for relief of nerve pressure. It therefore seems wiser to operate and relieve the nerve pressure first and if the patient still gets symptoms to do a second operation later for grafting and stabilizing the back.

THE DIFFERENTIAL DIAGNOSIS

The differential diagnosis seems to lie in these cases between —

- (1) The ruptured intervertebral disc, which seems to be common
- (2) A tumour within the spinal canal, which is rare. A spinal neoplasm can be differentiated by the progressive increasing signs of compression which are not seen with a disc, as a disc is a reasonably local affair and there is wide overlap between the neural segments
- (3) Spondylolisthesis, which will be shown by the lateral X-ray
- (4) A tuberculous lesion affecting the pedicles of the vertebræ. I have seen two such cases recently, but this must be extremely rare, and also seems to be associated with a chest lesion or with tuberculosis elsewhere

THE TREATMENT OF THE EARLY CASE.

If this lesion be accepted, and I think it must be accepted, as the most common cause of sciatica, it is necessary to be on the look-out for the early signs of the lesion so that such cases may be prevented from going on to operation. Crisp, at a recent meeting of the British Orthopædic Association, pointed out how these patients should be rescued from the massage department where they gravitate and are made worse by exercises and physiotherapy. If these cases are seen early and treated by immobilization in plaster jackets the condition can be cured at an early stage and further prolapse of the disc will be prevented. It would seem that such patients make a natural recovery. No patient should be operated upon until conservative treatment has been honestly tried, and if these rules are adhered to, unnecessary operations will not be performed.

OSTEOARTHRITIS AS AN ORTHOPÆDIC PROBLEM

By A M HENDRY, M B, F R C S Ed

Surgeon, Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry

A REDUCTION of the painful incapacity of osteoarthritis is one of the major problems of the orthopædic surgeon. An appreciation of the causative factors and efforts towards their elimination may achieve more by lessening the incidence of osteoarthritis than measures directed to the amelioration of the established condition.

PATHOLOGY AND CAUSATION

The pathological changes characteristic of osteoarthritis are softening and erosion of the articular cartilage, progressing slowly but steadily until the underlying bone becomes exposed and, by continued usage, sclerosed and polished. Concurrently, adjacent areas of cartilage become heaped up and an irregular marginal proliferation of cartilage and periosteal bone takes place, gradually widening the joint surface and forming projecting spurs or osteophytes. Some of the cartilaginous growths may become detached to form loose bodies. Although osteophytes may interlock and so render the joint immobile, fusion of the opposing surfaces never takes place. The changes are essentially degenerative. Inflammatory processes are not a feature of osteoarthritis, although a joint previously damaged as a result of an infective lesion is thereby the more susceptible to the onset of osteoarthritis. Nor is there any evidence that arteriosclerosis, focal sepsis, toxæmia of intestinal origin, metabolic or hormonal disturbances are factors directly concerned in producing the joint changes. They may act indirectly, since fibrositis, myalgia, obesity and a poor blood supply must adversely affect adequate muscle action and lead to ready tiring, so that joints in use become the more liable to trauma.

The researches of Bauer and Bennett (1936) and of Magnuson (1941) would indicate that the pathological processes of osteoarthritis are the result of the wear and tear of joints by repeated small, actively produced trauma and the stresses and strains of long continued use. Magnuson infers that cross-strains of the joint produce the typical changes, and suggests that the marginal tissue proliferation is an effort to buttress the joint against them. It may be that repeated trauma applied perpendicularly to the articular surface, especially during a movement of rotation, explains the case in which cartilaginous erosion predominates. Trauma occasioned by active physical use is more implicated than purely passive trauma. A joint subjected to the latter may become the more liable to the effects of the former. This view of the causation of osteoarthritis is substantiated by clinical observation. It affects the elderly from prolonged use, the middle aged and physically robust from excessive use. It predilects weight-bearing joints and those used predominantly by occupation. It appears at younger ages in joints ill-adapted to withstand the effects of ordinary use, such as congenital abnormalities, and joints the surfaces of which have become distorted by gross trauma or earlier conditions, such as Perthes's disease or slipped epiphysis. Congenital joint incongruity is the

most likely explanation of familial liability to osteoarthritis affecting the same joint, although some inherent abiotrophy of the articular cartilage cannot be excluded. Alterations in the line of incidence of stress and strain by coxa vara, knock knee, faulty alignment of fractures, bad posture and other causes of mechanical inefficiency, all tend sooner or later to its onset. Weight bearing is the chief exciting factor in the lower extremity and occupational trauma in the arm.

CLINICAL FEATURES

The clinical features vary in different cases, but bear a relationship to the pathological changes depending upon their extent and rapidity of development. *Stiffness* at the beginning of movement varies with an ache after use in the muscles controlling the joint. A difficulty in executing some movement, especially rotation gradually becomes a definite restriction, although seldom equal in all directions.

Pain is variable. It occurs early at the extremes of movement, from compression of the sensitive joint margins. Sudden acute pain may indicate the lodgement of a loose body or the impingement of a synovial tag hypertrophied by irritation of some marginal spike. When the cartilage undergoes a slow attrition, the underlying bone gradually becomes sclerosed and eburnated with an associated slow degeneration of its nerves, so that the joint may have a fairly wide range of movement accompanied by creaking and rough crepitus but with relatively little pain. In the absence of recent trauma the onset of pain in the elderly generally indicates an advanced lesion. Severe pain in the absence of marked bony changes suggests a rapidly progressing condition, such as is often seen in one hip when there are advanced changes and severely restricted movement of slow development in the other. The degree of pain may vary in the same joint from time to time, due to aggravation by injury or a period of excessive use. General tenderness of the joint margins also indicates an active phase. Pain induces muscle spasm which further restricts movement, and if unrelieved produces increasing deformity and contracture. Deformity and restricted movement in a joint increase the liability to trauma and so to aggravation. Pain for a time may be only on movement or on weight bearing, but later, especially when the hip or knee is affected, fixed deformity and muscle strain cause pain, often unrelieved by lying down, preventing rest and sleep, with consequent debilitation.

Osteoarthritis is slowly but steadily progressive. Being degenerative there is no power of recovery, but with adequate treatment the progress may be arrested, or at least retarded.

TREATMENT

In the consideration of treatment, the salient points to be remembered are that osteoarthritis is a degenerative condition caused by the repeated small trauma of self-inflicted stresses and strains, showing a slow but increasing progression and with no spontaneous power of recovery. Not involving any of the vital functions, it is consistent with long life, a prolonged period of which may be spent in relative misery. It affects the elderly who are unable to sustain severe surgical procedures, the physically robust middle aged who still anticipate further years of life in which they are naturally anxious to be active, and so they remain liable to the incidence of the causative trauma of osteoarthritis, and those of younger age with mechanical defects, to which the strains of a chosen occupation may be added. Further, an osteoarthritic condition in one individual may have an entirely different signi-

similarity from a precisely similar one in another, so that each must be considered by itself in relation to all its aspects, social and economic as well as surgical

General measures—General measures of treatment, such as the elimination of local sepsis and chronic constipation and the reduction of obesity, should be encouraged even though, as has been indicated, their influence is indirect. The various forms of physiotherapy, although at times beneficial, are but adjuvant. This applies also to the use of drugs.

Prevention—Essentially mechanical in production, osteoarthritis demands mechanical treatment. Attention should first be directed to the removal or mitigation, so far as is reasonably possible, of every predisposing or aggravating factor. The valgoid feet of babies, static and postural deformities of childhood, such as coxa vara, knock knee, bow leg, acquired misalignments and those due to growth defects, all should be corrected early. Cases of Perthes's disease or osteochondritis elsewhere should be relieved of weight bearing during the stage when the bone is plastic, so as to prevent distortion of it. In the treatment of fractures, clinical alignment no less than radiological appearances should be a criterion to prevent rotational valgoid and varoid deformities and consequent upset of the normal relationship of joint axes, minor degrees of which are likely to be more harmful than even greater ones of apposition and overlap. Local joint lesions, such as loose bodies and slipping menisci, should be removed, and recurrent dislocations, as of the patella, stabilized. Early recognition of avascular necrosis and adoption of suitable treatment, such as osteotomy of the femur at the hip or early excision of such a fragment of a fractured scaphoid, will lessen the liability to osteoarthritis in many cases, as will a timely bone graft for an incompletely reduced crush fracture of the spine.

The effects of such anatomical irregularities are obvious, less apparent and therefore more liable to be overlooked, although of equal importance, are the errors of use of normal joints. Faults of weight bearing are widespread and in themselves, as well as by augmenting occupational strains, are perhaps the most prevalent causes of osteoarthritis. Reference to the normal is necessary so that departures from it may be eliminated. On weight bearing the heel should be centralized under the leg and, with the first and fifth metatarsal heads, form a plane at right angles to the line of incidence of body weight through the leg. From this position dorsiflexion of the ankle should be possible. The knee should be fully extended and locked by internal rotation of the femur upon the tibia, a movement executed only by a full action of the quadriceps muscle. Simultaneously, the hip and lumbar spine should be extended by the gluteal and lumbar spinal muscles. The importance of fully establishing this position lies in the fact that once achieved, end-to-end weight bearing and stability are maintained without further conscious muscle action. Disturbances of the mechanism are many. When dorsiflexion of the ankle is not possible, due, for instance, to a shortened tendo Achillis, an eversion of the midtarsal joint and a valgus thrust on the great toe must take place as body weight passes over the foot on walking. Whilst the low heel of the male shoe does no harm, the far too prevalent pointed toe and unduly high heel of the average woman, causing her to place the tread on the ground even before the heel, greatly add to this thrust on the toe and tarsus.

The hip and knee are interrelated in weight bearing, flexion of one demanding

flexion of the other. When full extension of the knee is not established, continued voluntary contractions of the quadriceps and gluteals are essential for the maintenance of posture. This leads to ready tiring, progressive weakness, and an increasing lack of control of the joints. Body weight imparts a cross-strain on flexed hip and knee which, with a weakening control of the joint, explains the high incidence of osteoarthritis in women, most of whom, because of high heels or simply faulty habit, fail fully to extend the knee on walking. This effect becomes the greater in labourers accustomed to carry heavy weights on the back, and in those whose work demands prolonged walking on rough ground. A revolutionary change in women's footwear, although desirable, is perhaps too much to hope for, nor has the time yet come when men need not be beasts of burden, but the importance of proper weight bearing cannot be too strongly urged. In the treatment of osteoarthritis of the lower extremity, active contractions of the muscles at rest and bracing of the joints on walking should be encouraged, even when a retentive apparatus is worn, since they do not mean movement of the joints.

Weakness of the quadriceps and gluteal muscles will lead to incomplete extension of the knee and hip. This is prone to occur from stretching or disuse in relaxation in those whose occupation entails the maintenance of a flexed hip, knee and lumbar spine for long periods, such as miners, gardeners and heavy transport drivers. Similarly, almost every trade has its faulty posture or excessive use of certain muscles, so that the opposing ones tend to become weak. The importance of building up the muscles of the injured is now universally stressed. It seems rather unfortunate that an act of gross injury should be required ere this necessity is appreciated, whilst prolonged small trauma should pass unheeded. In these days when the efficiency of machines is demanded, surely that of the most highly specialized machine of all, for which there are no adequate spare parts, should be paramount. Insistence should be upon the maintenance of muscle power in health and opportunity and facilities provided to this end. A few minutes of each working hour should be directed to the performance of movements and assumption of positions opposite to those which the occupation demands. The time thus spent would not be lost if thereby an increase in working life were attained. Those, such as miners, whose working conditions preclude this hourly period, should have the facilities otherwise as part of their working time. This attention by the workman to himself should be as essential a part of his training as any other portion of his duty. As a further preventive measure, attention should be paid to guidance of the young, who have congenital or acquired joint irregularities, in the types of work to be avoided.

When the clinical features of osteoarthritis become apparent, treatment may be by manipulation, external fixation or operation.

Manipulation—In physically robust and younger patients a joint which shows a moderate restriction of movement and in which, apart from a possible narrowing of the joint space, bony changes are absent or minimal, may be manipulated under anaesthesia with benefit. Such manipulation must be gentle to avoid undue reaction. All movements should be carried out with particular attention to rotation. When the restriction is considerable, repeated small manipulations are preferable to one full one. Generally, manipulation should be avoided in the frail and elderly. Manipulation is not likely to improve a joint when restriction is

largely occasioned by muscle spasm and there is tenderness of the margins. After manipulation, proper use of the joint must be insisted upon and former aggravating causes avoided. If this is assured the improvement, both as regards movement and relief of pain, may persist indefinitely. If this is not likely to be so, a more permanent basis of treatment should be advised.

Rest and external fixation—There can surely be no greater fallacy in the treatment of osteoarthritic joints than that they must be kept moving to prevent stiffness. Little can be more calculated to aggravate the condition and its clinical manifestations. Rest of a joint by limiting its movement will relieve pain and lessen muscle spasm and, in consequence, reduce deformity not due to osseous causes. It is invaluable in mitigating the effects of an act of major trauma or exacerbation following excessive use. Rest may entail external fixation of the joint, which may be temporarily or permanently complete or partial. Its use may best be exemplified by its application to the knee joint. Extension of an osteoarthritic knee on walking causes nipping of the margins and especially of the infrapatellar fatty pad, consequent thickening of which renders it the more liable to further nipping. The muscle spasm which the pain of this induces increasingly adds to the deformity. Fixation of the leg in a plaster cast from the groin to the malleoli rests the joint. Muscle spasm disappears, and the thickening of the pad lessens, so that it is possible with further casts to obtain a straighter position. With proper bracing of the quadriceps on walking in the case, a final degree of almost full controlled extension may be achieved. Fixation of a joint should always be in the optimum position obtainable, and reduction should be gradually effected, plaster being replaced by less rigid supports. In cases with persistent pain at extremes of movement, when operative measures are not justified or contraindicated, some permanent means of external limitation is required. A raised heel alone will often serve to lessen pain in the tarsus, ankle or knee. Other cases may require a moulded arch support for the tarsus, a fixed brace for the ankle, for the knee a caliper or limiting cage which is best extended to the heel, for the hip a leather or other spica or a weight-bearing appliance, a block leather cock-up for the wrist and a fixed or limiting cage for the elbow, a corset for the sacro-iliac joints and a brace for the spine. Some patients with osteoarthritis of the hip, with even great deformity, obtain considerable relief, when more direct measures are contraindicated, by compensation of the apparent shortening by suitable elevation of the shoe.

Joint débridement—Magnuson has described the procedure of joint débridement and his results are encouraging, although the number of cases he reports are but few. It demands, however, a close selection of cases and the very full cooperation of the patient in after-treatment, which must restrict the general application of the operation. It may be that with the development of absorbable plastics this procedure may yet form the ideal for all joints.

Arthrodesis—The most certain means of relieving an osteoarthritic joint of pain is by arthrodesis, and were that the only consideration it would be the procedure of choice. It is more certain than external means of fixation, which also usually restrict other joints, thereby incapacitating the patient more than need be. Unfortunately, there must be other considerations than the relief of pain in one joint. Ankylosis of one joint may, in the elderly or physically active, throw undue strain upon some other and, although the stiffness of one joint may prove but

little handicap, in association with a later developed stiffness of some other, may produce an incapacity far greater than the sum of the two separately. Therefore before embarking upon a procedure just less radical than amputation, consideration should be given to the presence of, or probable development of, osteoarthritis in the opposite or some functionally related joint, and of the possibility of adequate treatment by operative or other means should that occur.

Joints which may be arthrodesed with reasonably good functional results, even when bilateral, the tarsus, ankle, the sacro-iliac and all three joints of the thumb, occurring singly or any two together; both wrists, although if there be limitation of rotation in the shoulders some difficulty in dressing may be experienced, one shoulder and one elbow but not on the same side. Unilateral or even bilateral arthrodesis of the knees may be demanded if pain is excessive despite external fixation, and if other means have failed. Arthrodesis of one hip assures a painless and stable joint, adequate for even the heaviest work. A mobile spine, however, is essential lest pain arise there later from the added strain thrown upon it. For this reason arthrodesis of the hip is best done relatively early in life.

Arthroplasty—Formal arthroplasty has but little place in the surgery of osteoarthritis. It generally achieves mobility at the expense of stability, and, although this may be accepted at one elbow when both are stiff, it is less satisfactory at other joints. Arthroplasty is less effective than most other procedures in the relief of pain in weight-bearing joints. Cap-arthroplasty of the hip may be considered when both joints are very stiff. The shock of the operation is apt to be greater than elderly patients can sustain, and the permanency of the result in the physically robust is not yet fully assured. Certain forms of partial arthroplasty often give helpful results—excision of one humeral head in bilateral cases, of the olecranon or head of the radius after fracture, of the patella in patello-femoral osteoarthritis, and of the proximal half of the phalanx of the great toe.

Other operations—Many other operative procedures have been advised, some of which have application in special cases. Of all the many operations advocated in the surgery of osteoarthritis of the hip, the *oblique osteotomy* (McMurray) is the one with the widest application. In cases of marked flexion and adduction deformity of the hip, a trans-trochanteric postero-external wedge osteotomy often gives complete relief by the altered incidence of body weight.

One operation which deserves more frequent practice is *remodelling the femoral head* as advised by Sir Robert Jones. It is simple, and if reasonable relief is not maintained, arthrodesis or osteotomy are still possible. I have just reviewed the case of a patient at the operation on whom in 1926 I assisted Naughton Dunn.

The man is now fifty-eight. For some years after operation he had a ninety degree range of flexion and still retains fifty degrees. Only recently has pain of any moment been experienced. In the intervening years he has worked as a stud groom, tramping many miles a day in the season, otherwise working as a coal delivery carter, carrying often three tons of coal a day, and he has served as a Home Guard throughout the war. An earlier appreciation of the causes of osteoarthritis might have prevented him inflicting this great strain on the joint with an even more lasting result.

References

- Bauer, W., and Bennett, G. A. (1936) *J Bone Jt Surg*, 18, 1.
 Jones, R., and Lovett, R. W. (1929) "Orthopædic Surgery," 2nd ed., Oxford, 258.
 McMurray, T. P. (1937) "A Practice of Orthopædic Surgery," London.
 Magnuson, P. B. (1941) *Surg Gynec Obst*, 73, 1.

CARCINOMA OF THE AXILLARY TAIL OF THE BREAST

By DUNCAN C. L. FITZWILLIAMS, C.M.G., M.D., Ch.M., F.R.C.S.

Consulting Surgeon, St Mary's Hospital, Surgeon to Mount Vernon Hospital for Cancer

MOST people, if asked to describe the breast, would start by saying that it was an organ with a rounded outline, situated in such and such a position. In this they would be entirely wrong for normally the outline of the breast is markedly pear-shaped, the tail of the pear being prolonged upwards and outwards into the axilla. In many cases the tail of the pear laps round the lower border of the pectoralis major muscle and lies in the axilla.

PHYSIOLOGICAL ENLARGEMENT

The extent of this axillary prolongation varies in different individuals. In some people a portion of the gland may be semi-detached and only united with the main body by fine ducts. In other cases a portion of the gland may become completely detached and may or may not have a tiny nipple of its own in the axilla. It is difficult to say if these detached portions are or are not supernumerary mammae. Possibly if they have a nipple of their own they may be, but those without a nipple, and therefore without the possibility of having grown downwards from the epithelium, must be part of the main gland which has become separated. These outlying portions may only become evident during lactation. Then the semi-detached portions form a swelling when the breast is turgid, which subsides when the milk is drawn off either by suckling or by artificial means. In the completely detached portions, secretory activity may cause a swelling to appear which will become painful, as no relief can be obtained. In such cases, cysts have been known to form which on tapping have yielded as much as a pint of milk. When a nipple is present, milk may flow from it and so relieve the tension. Often these portions of the axillary tail are symmetrical in each axilla. Champneys published an interesting paper on these swellings and, although his views were never accepted, and indeed since then have to a certain extent been proved erroneous, his paper is instructive to anyone interested in the subject.

Clinically, such cases are not uncommon, and those who see many breast cases come across a large number in the course of years. Typical examples of such are as follows —

Case 1. Aged forty-two. Seen 29.8.32

History. A swelling had been found by accident two or three months ago (probably more). This she thought was growing and lately she had begun to suffer pains in the breast and shoulder. Family history good. Has had three children, not nursed any of them.

Examination. There was an enlarged soft axillary tail on the right side, nothing to be felt on the left. There were no glands to be felt and there was nothing suspicious about it; probably it had always been there and had passed unnoticed. There was no shadow seen. Her mind was put at rest and she had no further pains.

Case 2 Aged twenty-six Seen 16 1 36

History She had found a swelling on the right side of her chest just inside the axilla, many years ago. Lately she had noted a similar one in the same position on the opposite side. She said that they affected slightly the movements of her arms. They had not grown larger she thought but they did enlarge at the periods, when her breasts became turgid. This made her a little anxious.

Examination There was a rounded, ill-defined swelling in the right axilla, which was freely moveable, tender, soft, not adherent to anything particularly. It was about 2 inches across. In a corresponding position on the left side was another similar swelling, rather smaller.

They were quite obviously semi-detached portions of the mamma, and she was advised to let them alone, take no notice of them, and set her mind at rest. She has had no further trouble with either.

PATHOLOGICAL CHANGES

Naturally these masses of mammary tissue have been reported as showing all the pathological changes which affect the parent gland, such as simple hypertrophy, abscess, and fibro-adenoma. Curiously enough, few writers have recorded cases in which carcinoma has been observed in these masses. The reason for this, however, may be that when carcinoma does occur at this site, it frequently remains undiagnosed until quite a late period, and therefore the result has almost universally been fatal. Fatal cases, if due to misdiagnosis, have a curious way of failing to find their way into print. From a personal series of such cases, the salient points of the condition can be usefully described.

The fact of the matter is that so little is this tail of the breast recognized that, when carcinoma does affect it, no suspicion of its serious nature comes to mind. It is sometimes mistaken for an enlarged lymphatic gland, and I have known a practitioner say that when he first saw it he carefully examined the breast to make sure that it was not due to an undiscovered primary mass in the breast itself. The idea that it might be the primary growth itself had never occurred to him.

SIGNS OF MALIGNANCY

The characteristics of carcinoma of this portion of the gland in the early stages are its hardness and its defined outline, as it has no surrounding breast tissue to muffle its shape. It is freely mobile. If the practitioner thinks it is of no importance, he will set the woman's mind at rest and she may take no further notice of the condition, or just think it is of no importance for many months, until growth or discoloration of the skin brings her again to seek advice.

Later on there is the attachment to the skin which occurs early, as the mass is very superficial. This should at once arouse suspicion as to its true nature, as this is a characteristic of malignancy. With time, too, the neighbouring glands become affected and enlarge. But even this may not excite alarm, as instead of one mass there may be two or more, all feeling hard and rather similar, and a common cause is sought without success. I remember one case in which there was rather widespread involvement of the glands, the preliminary diagnosis with which the patient was sent to me being an early case of Hodgkin's disease.

Later still, when there has been a spread to the skin, the typical plum-coloured discoloration takes place and can scarcely be mistaken for anything but carcinoma. But if the colour is red rather than purple, especially if softening has taken place,

It is quite liable to be mistaken for an abscess. Especially is this the case if the practitioner sees the condition at this stage for the first time. If the operator, failing to find definite pus, takes a portion for biopsy the diagnosis is certain. If, however, this is not done, further valuable time may be lost before the condition is recognized for what it really is (fig 1)



FIG 1

Sometimes, as the course is scarcely that of an ordinary acute abscess, a cold abscess is diagnosed and treated accordingly.

As the mass is superficial, ulceration may take place at an early date. The condition is then very difficult to treat.

TREATMENT

As the growth is not strictly speaking in the breast proper, the main portion of the gland can be ignored and left untouched, and attention confined to the region of the axilla.

Operative technique — The incision should be an elliptical one, removing the skin from over the mass. The incision is best made from before backwards across the axilla, starting over the lower border of the pectoralis major. The skin is undercut all round for the requisite distance and the incision deepened down to the pectoralis major. This muscle may be partially divided and will retract, exposing the pectoralis minor, which is retracted upwards. The fat and lymphatics are then divided at the apex of the axilla. With swab dissection all the fat and lymphatics are cleaned from the vessels and nerves, not forgetting the subscapular area. When the axilla has been cleared the pectoralis major can be joined up again with

catgut If there is any attachment to the pectoralis major a portion of the muscle must be removed, and then good union between the two portions may not be possible A stab wound is made through the skin and a drainage tube inserted

If *radium* is available, three needles, containing 3 mgm of radium mounted on copper wire (gauge 25), should be inserted along the axillary vessels, passing well behind the clavicle into the posterior triangle of the neck, and two more needles should be laid alongside the subscapular vessels After sewing up the wound gauze and wool are applied to form a pad in the axilla, and a figure-of-eight bandage is applied round the body and shoulder—what in Scotland is called the St Andrew cross bandage A many-tailed bandage cannot exercise any pressure on the axilla and should be avoided

The needles are removed on the third or fourth day, if left in longer they may interfere with healing

Two months later a small plaque of radium mounted on sorbo rubber may be fitted into the axilla, sheet lead must be fastened to the plaque to protect the arm This is fastened in place by strapping and should be worn for three weeks Constant care is needed to see that it is not displaced by the movements of the arm

THE ULCERATED GROWTH

If ulceration takes place, either because the condition has not been recognized, or after a faulty operation, the condition rapidly goes from bad to worse The ulcer penetrates deeply into the axilla Pain is the usual accompaniment of ulceration of any area where movements take place, and the thickened and inflamed walls of the ulcer rapidly begin to immobilize the arm and bind it to the side This leads at once to difficulty in dressing the ulcer, as free access cannot be gained to it As a result the odour becomes most pronounced and unpleasant and is evident to anyone entering the room The patient's life becomes one of misery, with constant pain, distress and anxiety, to which morphine is about the only answer

Treatment—Any attempt at radical operation is now almost out of the question Even under an anæsthetic it may not be easy to abduct the arm sufficiently to operate freely I know of one case in which previous to operation the arm was forcibly abducted, and the axillary vessels gave way Although these were secured after some delay the patient died, as gangrene of the arm set in

If seen in a fairly early stage, probably interstitial radium is the best remedy It is impossible to clean the ulcer satisfactorily, although filling the cavity with sulphanilamide powder may do good Under the anæsthetic the larger slough may be cleared away, but gentleness should be used, as the relation of the ulcer wall to the vessels can only be guessed The ulcer is packed with gauze filled with sulphanilamide powder Needles 40 to 60 mm in length should be used containing 2 and 3 mgm of radium respectively These are thrust up parallel to the walls of the cavity and about a quarter of an inch from the edge, so as to be at what is judged to be the edge of the malignant tissue They are placed about $\frac{1}{4}$ of an inch apart They cannot be placed on the outer side because of the vessels It is a good plan to place a well-screened tube of 20 or 30 mgm of radium in the ulcer itself This should be mounted on stiff copper wire which is fastened to the chest with strapping and can be moved when needed, the stiff wire preventing

ts being displaced by movements of the arm. The needles and tube can be removed at the end of a week. An overdose of radium is almost impossible in the case of ulcers. The object is to destroy as much of the malignant tissue as possible so that a certain amount of healing will take place. Great improvement takes place, the ulcer becomes cleaner, smaller and less deep, many have healed completely.

Unfortunately the radium causes a lot of fibrosis and, as a result, the arm becomes more than ever bound down to the side, and renders access to the ulcer most difficult. The swelling of the arm, which must in these cases be pronounced, is aggravated and tends to get worse as the fibrosis presses on the veins and obstructs the lymphatics.



FIG 2

In one case, recorded below, in which the growth had been opened under the impression that it was a cold abscess, the improvement of the ulcer either from radium or from injections of H 11 was so marked, with the consequent drawbacks already referred to so evident, that the patient decided to have a forequarter amputation performed. As a result she got rid of the local part of her disease entirely. Time will show if it has or has not already been disseminated through her system, but the freedom from pain, absence of odour, and the patient's belief in cure have had such an effect on her general health that she is now a different person. It is a curious thing that although I have seen a good many people who have had forequarter amputations, I have yet to meet the person who regretted having had it performed. The patient certainly looked peculiar when showed to the Clinical Section of the Royal Society of Medicine, for she had had the fore-quarter amputation performed for carcinoma of the breast, and yet she had both her breasts intact (fig 2).

I have among my notes some thirty cases illustrating this form of carcinoma, but space will not permit of more than six being published. I have therefore

selected six cases, in five of which death resulted in the manner described in the text. The only one who survived was the patient who underwent the forequarter amputation.

The paper has been written to point out the seriousness of the condition, hence the selection of cases.

Case 3 Aged fifty-six Seen 18 9 26

History Three months ago injured her breast against the bed-post. The pain lasted for some weeks and then passed off, but returned recently and she then noticed that something was altering the shape of her breast. She came of a long-lived family. She had had seven children and nursed them all for more than one year.

Examination A deep pucker ran up from the axilla across the lower border of the pectoralis major, and the skin was bound down over it and over the upper and outer part of the breast, so that the nipple was slightly displaced outwards and upwards. The skin was thick all over the axilla but glands could only be felt along the subscapular vessels.

A radical operation was performed in St Mary's Hospital. At the operation it was evident that the case was inoperable and should never have been touched by the knife. All the muscles were infiltrated with growth and œdematous, the axilla was a mass of glands. The operation undoubtedly helped to spread the growth. The wound healed but the growth reappeared rapidly in the axilla. She died in the beginning of November, 1926 (in less than two months).

Case 4. Aged fifty Seen 5 3 29

History In September, 1928, noted a hard lump in her right breast near the axilla. This she fomented and at Christmas it broke and had never healed.

Examination There was an ulcer about $2\frac{1}{2}$ inches across with very hard, high, walls which stood up about $\frac{1}{2}$ of an inch and were about $\frac{1}{4}$ an inch thick. Behind it was a hard mass. It was situated on the anterior axillary fold and obviously affected the very tail of the breast. Sloughs covered the base of the ulcer. Interstitial radium was given and a tub of 30 mgm was laid upon the surface of the ulcer and moved daily. In all she had some 8,024 mgm hours. In April 1929 the ulcer was much smaller and shrinking fast. By the middle of May it was almost healed but her general health had deteriorated from internal metastases and she died in June. By then the ulcer was quite healed.

Case 5 Aged forty-nine Seen 23 4 30

History Two years ago a "swollen gland" came in the right axilla, and this persisted. One year ago Mr. Rose of Derby put radium needles into the swelling. Since then there has been a persisting, discharging ulcer in the axilla, difficult to treat. There has been no pain, no cough, and her general health is good. A year ago the arm began to swell and the movements became limited owing to the ulcer.

Examination Looks well and is fat. There is an ulcer about an inch across in the axilla which extends deeply, surrounded by inflammatory and cicatricial tissue. X-ray shows no secondaries in the chest.

28 4 30 The ulcer was surrounded by needles of radium and an interstitial dose of 6,552 mgm hours given.

20 5 30 The ulcer is smaller, more healthy, but is still deep and foul smelling.

19 6 30 A radium tube of 25 mgm of radium was put in the ulcer and a dose of 300 mgm hours given. The ulcer began to heal more quickly but was still deep. Slight improvement went on up to 2 8 30, when there was severe axillary hæmorrhage which was controlled by plugging. Four days later there was another sudden profuse hæmorrhage from the long thoracic artery and from a large intercostal artery which could not be controlled and she died in two hours. The source of the hæmorrhage was ascertained post-mortem.

There was a question as to whether the growth was a carcinoma or an epithelioma. Two sections were taken. The report on the first said it was probably derived from squamous epithelium but was not certain. The report on the second section mentioned spheroidal, polygonal and cubical cells, no keratinization was found. "The origin of the growth is therefore uncertain."

Case 6 Aged forty-two Seen 19 8 42

History Three years ago a lump formed in her right axilla. A practitioner told her it was nothing and she need not worry. This grew but the practitioner still said it was of no importance. She then went to a surgeon, who thought it was a cold abscess and drained it.

CARCINOMA OF THE AXILLARY TAIL OF THE BREAST 101

it did not heal, a further operation was undertaken. It discharged for some time, then had deep X-rays and the condition got better, but then broke down again and discharged ever since. She had more deep X-rays without effect. In February 1942, she had a small dose of radium without improvement.

Examination The left upper arm measures 10 inches whilst the right measures 13 inches. There is a discharging ulcer in the axilla, which is difficult to see owing to the adducted position of the arm. The breast feels a little stiffer owing to lymphatic engorgement. She has not lost weight.

23 8.43 She had needles containing 3 mgm of radium inserted all round the deep ulcer, which went right up nearly to the top of the axilla, about 7,000 mgm hours. She was given stilbæstrol but it made her sick and had to be stopped. A 50 mgm tube of lum was kept in the ulcer and moved about daily. She was given H 11 as directed on instructions. After a time she seemed to improve, and although there was a great deal of pain her general health was better. In November she was well enough to go home attending her H 11. She got well, but the arm was so painful and such a nuisance, as the left arm did nothing but nurse the lame one, that she asked for it to be removed.

10 1.44 Forequarter amputation performed, the subclavian artery was found occluded and empty, but nothing special was noted in the collateral circulation. She went home 2.44, after being shown to the Clinical Society as a curio, having had the forequarter amputation for carcinoma of the breast yet she apparently had both breasts intact (see fig. 2).

June 1 had a letter that she was in good health and doing her own shopping.

25 5.45 The patient has gained weight, is well, and is carrying out her household duties.

Case 7 Aged forty-seven Seen 15 31

History In October 1930 noticed a lump under the left arm, now there is another near it the breast. Both are painful and have been so for two months. The mass in the axilla is always painful when she had her four children.

Examination Indefinite lump, the size of a walnut, far out in the upper quadrant of the breast, extending into the axilla. Shadow not well seen but is there. Massive glands in axilla.

6 5 31 Radical operation, as the mass was well into the breast.

Pathological report Alveolar, tubular and trabecular columnar-celled carcinoma with metastases in the axillary glands. The growth is forming much mucin, giving it the appearance of a so-called colloid cancer. The fibrous reaction is slight and mitotic figures are frequent. In July she had surface radiation, 12,760 mgm hours.

She died in March 1932 of secondary masses in the chest, and the end was due to pneumonia.

It would be difficult to receive a more menacing pathological report as regards prognosis, and she was dead within the year.

Case 8 Aged sixty Seen 19 5.44

History For the last three weeks has known she has had two lumps in her left breast. Nothing of note in the family history. Has had two children, and nursed both with no breast trouble.

Examination Stout woman with ample, pendulous breasts. The right is normal. In the extreme axillary tail of the left breast are two lumps which feel almost like lymph glands. The skin is beginning to be attached over them, there is a firmness in the axilla. Near the outer side of the nipple, deeply situated, something very indefinite is felt, quite mobile and no real shadow cast.

5 6.44 Partial removal of the breast in the Royal Masonic Hospital. A primary lump was found in the tail of the breast and the next lump was a gland. Glands extended right up to the first rib and were attached to the vein. It was impossible to get them all away, so they were cauterized and interstitial radium was put in, 1,298 mgm. hours. It was obvious that she was really inoperable.

Pathological report The growth was a rapidly-growing carcinoma with numerous mitotic figures and pyknotic nuclei, which has widely infiltrated the fatty tissues and the glands. Numerous necrotic areas present.

The amount of radium inserted was quite inadequate to destroy the growth remaining but was still large enough to delay healing and when she left the hospital she still had a sinus.

26 9.44 Her husband wrote that she had been admitted to the Salisbury Hospital. She died shortly afterwards.

BITES AND STINGS

By C. G. LEAROYD, M R C S, L R C P

THE stings and bites that vex the skin of man in this country may be divided into two groups—that in which man is the aggressor or at any rate runs up against a defensive mechanism, as in the case of bees, wasps, stinging nettles and weever and that in which he is the victim—mere bug, louse or flea fodder. Nor is the consideration of these troubles on man's frontiers merely one of entomology or piscatology and the appropriate pharmacy, it is much more than that. It is the study of contacts, varying from almost intimacy to the clashing with strangers for some were known of old to man's forefathers, comprising even one of the plagues of Egypt, and there are dangers in his very habituation to them. Some he quietly and competently neutralizes at source, some are comparatively new to him, and to these he may offer the resistance of the macule or papule or the barne of the wheal, some he has to master again each season, some he meets so rarely that he has no special defences against them, and a few are so rare and so deadly or so individually poisonous, that all he can do for the moment is to fall back and keep his essential services running as in shock. Therefore not only man and his lowlier brother creatures must be considered, but their previous relationships as individuals and racially.

THE LOUSE.

Taking the aggressors and man's oldest intimate first, it may be noted that the human louse, a wingless insect, has two local varieties, the body and the head louse. They interbreed freely under experimental conditions, and the cross-bred are fertile. Moreover, when *capitis* is reared under conditions congenial to *corporis* it loses its distinctive characters. There is reason to believe that *capitis* is the more primitive race and that *corporis* was derived from it when the host took to clothes (Imms). Their habits, however, are different.

The body louse (*corporis*) lives by choice on the inner side of the underclothes, lays her eggs there, or preferably in the cooler outer clothes, and goes on to the body for meals. Hence the upper parts of the shoulders and buttocks, being in closest contact with the underclothes, are the favourite sites for feeding, and hence scratch marks are nearly diagnostic. Most people in the Middle Ages had lice, the adjective "lousy" being earned only when they were in abundance. They are even now sometimes found on people of good social position, when the tact of the physician is tested in getting rid of them and not upsetting their host. The observance of the weekly bath and change of linen will keep the louse population down to a few brace and this may go on for years. It appears certain that lice leave a febrile patient and seek another host, and since two Rickettsias, of typhus and trench fever, are transmitted by the faeces of an infected louse, and the spirochaete of relapsing fever by the blood of a crushed louse infecting a scratch, this is of the utmost importance. Moreover, they are fair movers. Nuttall timed a female over a metre on black sateen and found she did it in 2 minutes 43 seconds. Of course, this touchiness of the louse to the greater heat coming from man's central heating may not be the only reason for their exodus, the quality of the food may not have

en up to standard, but it does show how dependent the louse is upon normal man and suggests how age-long has been their association

The life of an adult is one month, during which time a female will lay some 50 eggs. It obtains its food by puncturing the skin with a proboscis and sucking out the blood. The bite is rarely visible as a minute, red papule which is said to irritate greatly, but usually it does not. The majority of people who have lice seem unaware of any irritation and in quite a number of the minority it only makes enough impression to give rise to a little subconscious scratching. I was with a number of other young men in France during the 1914-18 war when they found that one of their number was lousy. They were upbraiding him for his uncleanness when they became introspective and found that they all had lice. Man seems to recognize that his tactile sensation is an uncertain warner, for he will often itch more from seeing lice, or even reading about them, than from the bites themselves.

To get rid of body lice is a simple matter—a hot bath followed by anunction of sulphur ointment or 25 per cent. xylol in equal parts of lanoline and petroleum jelly will account for lice and any eggs that may have been laid on the body hairs. The disinfection of clothing is of far more importance, and is generally done by heat or steam or soaking in petrol. In future DDT will probably be used, 1½ ounces of a 10 per cent. dust puffed through openings in the clothes will delouse and keep deloused a man in winter clothes, which must not be washed, for three weeks or more. Impregnated clothes which will resist several washings are effective. It is not ovicidal, but its long, lingering poison makes up for this defect.

The *head louse (capitis)* lives on or near the scalp and the eggs are laid chiefly on the back and side hairs near to the scalp, where as a routine they may be looked for (together with clubbed fingers) when ruminating with a stethoscope on the back of the lungs. Viewed without prejudice the "nit" is a work of art—a pearl-grey, lidded chalice, enshrining and jewelled by the egg, is attached by a delicate but immensely strong handle to a hair, from which it can be loosed only by being slid to the end. Later, inside the chalice is a delightful mechanism for eruption: the larva swallows air and passes it out posteriorly, making a pressure-chamber as in an air-gun until the time of its deliverance is accomplished, when it acts as in jet propulsion.

K. Mellanby, that Cortez among the ticks, mites, and insects, found in ten industrial cities that 50 per cent. of the girls and 27 per cent. of the boys between the ages of two and thirteen were infected. No wonder that a high-brow and a sanitary conscience are no safeguards against this insect. Enlargement of the posterior auricular and cervical lymph glands, or impetigo of the scalp or back of the neck, should always rouse the hunt. These, of course, come from secondary infection, which seems to cause far more itching than the lice themselves. Indeed, head lice would be much less common if they itched more, and natural selection is ever weeding out the more irritant.

For very young children who cannot resist the indignity of a hair crop, that and dilute ammoniated mercury ointment are all that is required. For the older patient the simplest method is to soak the scalp and hair thoroughly with methylated spirits seven parts, water three parts. Then on the wet hair put a rubber bathing cap for two hours, when the hair dries quickly and the nits can be combed out. Whitfield's method was to soak the hair in 1:40 carbolic and turban the head in

a towel for two hours Both methods kill lice and ova, but forget not the hat, cap, and pillow-slip A method of prevention and cure, used in the Services, utilizes the organic thiocyanates and laurates, e.g., "lethane 384 special" This is mixed, half and half, with liquid paraffin and scented An application of from 30 to 60 minims, according to the bulk of the hair, is dropped through partings on to the scalp and spread by massage The head should not be washed for ten days. D D T, 0.2 gm., completely louse-proofs the head for a week (Busvine)

The *crab louse* (*pubis*) is not such an elongated insect, in fact it is as broad as it is long, the sort of build generally associated with a scrum-half, its characteristic stance, too, with legs wide apart, clutching hairs and mouth parts buried in the host, is reminiscent It does not gorge itself and go away like the other louse, but keeps in this position and apparently sucks intermittently as through a straw It is not known to carry any disease, but it is itself often conveyed by sexual intercourse The "maculæ cæruleæ" are bluish plaques of $\frac{1}{2}$ to 1 cm. in diameter They are said to be produced by a pigment injected with the saliva of the louse, and occur on the inner surfaces of the arms and thighs and the side of the trunk in fair people They may be compared with the secondary rash of scabies and other sensitization rashes, which seem as though they were man's patterned attempt to deport a toxin

To get rid of these adherents the simplest way is to shave off the affected hair and then apply the 25 per cent. xylol ointment for a few days and not to forget the peri-anal hair The practitioner is as a rule warned against the old-fashioned "blue butter," ointment of mercury, but I used it for ten years at sea and had only one case of dermatitis from it If the growing pains of pubic hairs would be resented, the methylated spirit or carbolic treatment as used for head lice may be employed for an hour, then the nits removed with a tooth comb, and the xylol ointment used for a week for chance survivors

The bite is said to cause much irritation, but this is by no means always the case I examined a regiment of young soldiers on board ship going out to the Near East and found over forty of them infected, some heavily—even unto the sternal hairs These men had had every opportunity of reporting twice a day for ten days and yet not one of them had done so To nearly all, their condition came as a complete surprise Of course, once these insects are known to be present other nerve tracks bear messages of itching to the cortex "How could I have lived without itching?" says a haughty voice, dimly recognized as belonging to the psychologist's super-ego "You don't suppose I am used to them!" No, but your fathers were and for a thousand generations, and although *P. pubis* is more irritating than *P. humanus*, there is not much sensitivity to either of them, neither does the skin answer as tartly as to a nettle-sting

SCABIES

It is interesting to compare the power of the louse to irritate man with that of the war profiteer, *Acarus scabei* By far and away the most important point in the life history of this mite which causes "the itch," from a medical, entomological and its own point of view, is that when it is attacking virgin soil, i.e., a person who has not had scabies before, for the first month or two, and sometimes much longer it does not itch at all That is the salient and pivotal fact about scabies, and failure

to recognize it is like being ignorant that a neighbouring nation is mobilizing "Actually it is possible for people to have mites burrowing actively in their cuticle for weeks without causing the least sensation. Not only is this possible, but it is apparently a universal occurrence at certain stages of every person's infection with scabies" (Mellanby's Oxford War Manual "Scabies") When it is borne in mind that the newly-wed female can do the inch in a minute, that she takes only an hour to bury herself in the horny layer of the skin, that within a couple of hours she is laying her enormous eggs at the rate of two or three a day, that these hatch out in three days and the larvæ run out of the burrows to hide in the hair follicles to become mature in a fortnight, that all this goes on for a month to six weeks without causing the slightest annoyance to the host, is it any wonder that in spite of a 90 per cent. infant mortality the acarus thrives? Then after this lengthy period, suddenly the host wakes up to this peaceful penetration, becomes sensitive, and begins to itch. If he is cured—and the cure of the plain, individual case of scabies is a simple matter—and then gets infected again, as he very likely will be if the whole household is not dealt with simultaneously, he will immediately itch, and may indeed end this second infection by scratching out the mite.

Another important, but not so important, point about scabies is that nine out of ten people with scabies have burrows on their arms, the feet, penis and scrotum, buttocks, and axillæ come next and in that order, the distance between first and second being considerable. In approximately 900 male cases Mellanby found that more than half had under six burrows, only three had over fifty, the highest score was 511, and the average 11. How typically English! Another important point is that the characteristic red, follicular and papular rash on the axillæ, the belt line, and the inner sides of the thighs does not correspond with the sites of the burrows nor does its intensity correspond with their number.

A word about the itching at night, which Mellanby has shown is not caused by nocturnal burrowing, as was thought. Many skin troubles are more irritable at night, chilblains and senile atrophic states are notorious, but scabies seems to be the worst. One factor which must not be overlooked is that when man goes to sleep there is a regression of sensation—sight fades, hearing dims, and for a while tactile sensation dominates the consciousness. It is not unreasonable for an animal to take cognizance of his immediate surroundings just before becoming defenceless. All patients should be warned that the itching may continue long after cure, otherwise they may continue with the lethal therapy and get dermatitis.

The treatment for this itching after cure is a zinc cream containing a 10 per cent solution of coal tar and the reassurance that the mite indeed is dead and that his tickling poison will go too. The two standard ways of treating scabies, with sulphur ointment and benzyl benzoate, are eminently satisfactory if the proper ritual is followed, and are too well known to detail here. Benzyl benzoate is an ingredient of Peruvian balsam, and Balsam of Peru, 60 minims in 1 ounce of 12 per cent. zinc cream (Roxburgh) is useful in children, those with eczema or secondary infection, and may be used for a week.

Animal scabies from cats, dogs, horses and camels often attack man. The mites do not burrow, the skin reacts at once with a red papular rash, and they are easily got rid of with sulphur.

Other mites closely related to acari are present in grocery—cheese, meal, dried fruit, and linseed oil the skin will react to them in a number of ways, from the treble of the macule to the bass of the angry wheal or the prolonged discord of dermatitis

FLEAS

Record high-jump, $7\frac{3}{4}$ inches, long-jump, 13 inches! (Mitzman) 'Dog, cat, and rat fleas bite man *en passant*, but do not stay, *P. irritans*, although it prefers man, is often found on fox and badger The flea voids and regurgitates at meals—hence plague The bite shows as a minute hæmorrhagic bulls-eye in a pink target, but many people give no reaction or are not bitten It seems as though the amount of antibody in the blood regulates its palatableness to the flea. Fleas breed in cracks on floors, so repellents, such as the paralysing pyrethrum or the smelly ones, should be applied to the legs Dimethyl phthalate, an oily liquid with a future, can be used on the skin or to impregnate clothes and is a much more lasting repellent. When D D T is released the civilian bugs and fleas are going to have a bad time

BED BUGS

Elizabethan immigrants with a stink, but few have got used to them yet and they generally leave two or three conical papules Some old observations of mine in the half-light of a Murmansk hut suggested that the sudden sting is a delayed action affair, and that is why the turn out to hunt at night is often unsuccessful. The bed bug is accused of transmitting kala-azar and relapsing fever, and three personal experiences suggested that a violent form of mumps with early complications may also be bug-borne An anti-pruritic shake lotion of 1 per cent phenol and 5 per cent menthol in a calamine lotion mollifies the irritation of bug and flea bites The bug feeds on blood alone, but can easily beat the professional faster

Harvest bugs six-legged larval forms of a variety of acarids, normally parasitic on small mammals Scarlet in colour they lie in wait on the grass Reaction is an intensely pruritic papule with a pink halo From experiences in a number of boys' camps it was noted that most boys were never troubled and that the same boys were bitten year after year The season is July–September, but one mite did not observe the "close-time" and bit Roxburgh on November 5! Another delayed action bite—two hours' delay, then the violent irritation increases for thirty-six hours Protect by dusting 5 per cent. sulphur in talcum powder on socks, or stockings or by smearing legs with sulphur ointment. Dimethyl phthalate socks will probably be the safeguard of the future Remove the mites with benzine, petrol or salt water great sufferers should carry benzocaine, 2 gm in 15 c cm flexible collodion, in a bottle with a rod stopper Eastern *Trombicule* convey Malayan scrub typhus

If man is the home of the louse, the hotel of the flea, the restaurant of the bug, for the next two classes he is mere caviar—an occasional luxury!

HORSE-FLIES

Tabanidæ—Five genera and twenty-one species, are British Only the female bites; the male is a vegetarian Specializes in silent approach and produces a sharp, rousing bite which may go septic

GNATS OR MOSQUITOES

ulicæ—Only the females again! According to Manalang it is the product of the salivary glands and the œsophageal diverticula that causes the reaction. People who become immune to one species of mosquito may not be so to another; there are twenty-nine to try out in Britain, but several are not convicted of blood-sucking, and against one of the *Theobaldias* there is but a single charge—of biting an inhabitant of Tunbridge Wells! The mosquito transmits many diseases, but is not important in that respect in this country—at the moment. Large blebs may result from the bite, especially on babes. D D T kills gnats and larvæ and will render large portions of the earth's surface more habitable. As little as 0.1 c.cm. of kiesel oil containing 5 per cent. D D T per sq. yard killed all larvæ and continued to kill them for four days. There are a number of new repellents—indalone, Rutgers 612," besides dimethyl phthalate—which are variously and specifically much more efficient than the old ones.

It is with relief that I turn to those bites and stings in which man is the aggressor, although it is sometimes hard to say who started it.

BEE STINGS

Bee stings may cause death. The venom consists of formic acid and an organic base which forms "a connecting link between the snake poisons and cantharadin." Apparently it is the partnership that gives the kick to the sting; each constituent alone seems fairly innocuous. When serious results occur the reason may be geographic, e.g., a person is stung in the fauces or the venom enters a superficial vessel, or chemical—an extraordinarily virulent bee or an anaphylactic man who rumbles at the venom, the bee's proteins or contaminating pollens. It is significant that when serious results follow there is little or no local reaction. Bee-keepers become partially immune and give a precipitin reaction, the human body manufactures an antiserum in twelve days. They may have to repurchase their immunity each season. Occasionally old bee-keepers suddenly become sensitive. Bee-stings apparently benefit certain types of rheumatism, but whether this is a protein shock reaction or something more specific, or occasionally even a reaction to fear, is not known.

The first-aid treatment is to refrain from pulling out the sting, as more venom would be injected. Edge it out with a knife and apply an alkali—ammonia, sodium bicarbonate, or even soap. Anaphylactic symptoms should be treated with adrenaline, intravenously if necessary, and in the same way as for other forms of shock.

WASP STINGS

Connoisseurs say this is a few volts more painful than that of a bee. Two deaths were reported in *The Lancet*, 1941, one in 20 minutes. An American soldier who became unconscious after a sting said that his last sensations were that his skin "was popping all over," and a boy who became drowsy after a sting developed generalized urticaria. There is little cross-immunity between wasp and bee stings. The venom is a highly complicated substance containing a volatile oil, choline and tryptophane, another authority adds a spot of histamine. It is alkaline or neutral in reaction. The cure of waspishness is acidity—generally vinegar!

Hornet stings—Acids, alkalis, and potassium permanganate are severally recommended. Try all three!

POISONOUS FISH

The poisonous fish around the British coast are by no means to be ignored and the *Lesser Weever* is the most important. The poison comes from the gland at the base of the dorsal spines and the spine at the back of the gill-covers, both of which are grooved. It is by far and away the most painful sting in these isles; it makes strong men weep or maniacal. Muir Evans reports several deaths, and the stung arm of a victim whom I saw on the Dogger was like a thug. Paddlers and shrimpers are liable to tread on the black fin protruding from the sand and fishermen to get stung when sorting the haul. The *Greater Weever* is more common on the West Coast, the *Father Lasher* and *Spurdog* also have poisonous fins. Even the little spine by the vent of the mackerel is poisonous at times, as Muir Evans has shown.

Early first-aid treatment is dramatic in its relief of pain; it consists of ligature of the part and the getting of potassium permanganate to the poison, either by solution (5 per cent.) in a hypodermic syringe or by splitting up the bite and rubbing in the crystals; the pain is such that these little manoeuvres will not be noticed. An antiserum has been made.

ADDER BITES

This handsomely marked reptile with gentle eyes and a lovely blue belly occasionally has to squirt the modified secretion from its parotid down its canalized teeth into blundering humanity, and unless the victim happens to be a snake charmer and to have been bitten repeatedly by the young of adders, the result may be serious.

The first-aid treatment is ligature of the digit and/or the single bone, i.e., the femur or humerus. Then wash the skin around the wound, as venom is often left on the skin. Then suck and get potassium permanganate to the venom as soon as possible. Every practitioner in adder country might well learn where to lay his hands on antivenine, even on a Bank Holiday.

CONCLUSION

This ends the sketch of an ever fluctuating relationship between man and his other holders of life who are associated with him on these isles, one that is probably less intimate now than of old. Does man get anything out of it? Are there any collateral advantages to be obtained from achieving immunity against some or any of them? Are men who get immune to nettles—and some do obtain a partial or a local immunity, on the knees when wearing shorts, for instance, or very rarely may have a congenital immunity to this poison which does not seem to be accurately known—do they, to take a disease at random, get gout? If there are any specific side-effects like this, they do not seem to have been worked out, but I have often wondered when seeing boys off, fit and forceful after a camp, how much of this vigour is due to the air, the food, the exercise, and how much to the thousand nettle-stings, the hundred gnat bites, the wasp sting or two.

To one who has wandered come voices from parallel worlds, and one sentence from a Scotch commercial traveller, laying down the law in a ship's smoke-room still rumbles. "It isn't the respectability of a firm nor its reserves that show whether it is a flourishing concern"—an index finger wagged in simple earnestness—"nay, it is the turrn-over."

SOME STATISTICS AND A REVIEW OF A YEAR IN GENERAL PRACTICE

By D R SNELLGROVE, PH D, M Sc, A R I C, M R C S, L R C P

THE following records are for the period September 1, 1943, to August 31, 1944, and refer to the practice of one member in a partnership of four, with his own panel of about 2,000, with approximately the same number of private patients (this was the first year of the member in the partnership) The surgery premises, which were erected for the purpose in the practitioner's garden and are separate from the house, consist of a large waiting-room to seat thirty, a consulting-room and a dispensary; all heated by a hot water system of pipes and radiators The practitioner's wife, a State Registered Nurse, acted as nurse receptionist and did most of the dressings, assisted with the dispensing, kept the appointments book, gave some injections, answered the telephone and immeasurably helped in innumerable ways The accounts were kept by the partners' secretary

TABLE 1

	Total	Consultations	Daily averages in whole numbers
Surgeries a m	289	7,547	26
" p m.	237	6,021	25
" afternoon	182	987	5
Total surgeries	708	14,555	47
Visits	3,877	—	12
Night calls	47	—	—
Total of surgeries and visits (310 days at work)	—	18,479	60
Written prescriptions	11,423	—	36
Certificates (all types)	8,675	—	28
Letters (re patients and practice)	410	—	1
Total of prescriptions, certificates and letters	20,508	—	66
Dispensings	2,821	—	9

The surgery has opened for 289 days and in all there were 708 surgeries Hours for consultation were 9 a m to 10 a m, 6 p m to 7 p m, daily, except Sunday and Thursday evenings, and by appointment 2 p m to 3 p m daily, except Thursday and Sunday The total number of consultations was 14,555 and the total visits

were 3,877. The largest surgery was 57, on December 4 in the morning; the largest number of visits was 28, on December 6, the smallest surgery, morning or evening, was 12, on August 9. There were 47 night calls, which included 3 in one night. The number of prescriptions written was 11,423, the number of letters was 410 and the number of medicines dispensed was 2,821, many private prescriptions being made up by chemists. A reference to table 1, which summarizes these records, will show that on 310 working days an average of 60 patients were seen, and an average of 66 prescriptions, certificates and letters written.

TABLE 2

Anæsthetics	87
Antenatal examinations	52
Aspiration (bursa)	12
" (ganglion)	5
Coagulation time	6
Dilatation of prepuce	32
Dressings	518
Ears syringed	120
Foreign bodies removed from eye.	41
Full blood counts	28
Hæmoglobin estimations	41
Injections	812
Microscopical examinations	91
Minor operations	28
Number of births	9
Paracenteses	21
Patch tests (for tuberculosis)	8
Pathological specimens sent	30
Pessaries fitted (watch spring)	6
Repair of perineum (midwife's calls)	8
Sedimentation rate estimations	56
Skin tests	13
Sutures inserted	32
Sutures removed	71
Transfusions	3
Urine analyses	297
Vaccinations	5
Varicose veins injected	58

Table 2 collects together some of the various activities of general practice. It is interesting to consider and explain a few of these. One of the transfusions was plasma, given for post-partum hæmorrhage and shock, to a patient who also had inversion of the uterus (she did well), another was for a dehydrated patient in a caravan. Some of the microscopical examinations consisted of blood films for differential counts, centrifuged urine deposits, skin sections, sputum, vaginal smears, fæces, hairs (for tinea) and the hunt for scabies. The sedimentation rate was estimated as a routine for tuberculous and rheumatic patients and in some obscure cases. The practice is in an industrial district, and foreign bodies in the eyes are common. Skin tests were used for asthma, allergy and for a few dermatological conditions. A patient with inoperable carcinoma of the ovaries and extensive secondaries, and a young girl with mitral valve trouble and congestive heart failure were tapped frequently. Minor operations consisted of removal of sebaceous and Me-

bomian cysts, moles, plantar warts, toe nails, myringotomy, thrombosed piles, circumcisions, and opening of abscesses. All dressings that can possibly be done there are dealt with at the surgery. Injections include those for varicose veins, pernicious anæmia, whooping-cough and diphtheria (passive and active immunization), tetanus (prophylaxis) and a large number, using procaine, for some rheumatic conditions, e.g., lumbago, fibrositis, sciatica, and for fractured ribs and sprains. Hæmoglobin estimates were made routinely in all pregnant women (Gower's method). The 87 anæsthetics include dental gases, ethyl chloride, sodium pentothal and open ether. Only eight patch tests were done for tuberculosis. The number of ears syringed, 120, seems large, but this was never done unless on otoscopic examination it was found to be necessary, and in each case the wax was "softened" for at least two days with sodium bicarbonate ear-drops (N.F.). The nine births include one set of twins. The total figure may seem low but there is an excellent Municipal Midwives Service in the town and also a Borough Maternity Hospital.

For the purposes of the classification of diseases no patient is entered under more than one disease unless seen for a different disease on another occasion, and the figures take no account of the number of attacks or relapses or exacerbations.

DISEASES DUE TO INFECTION

In the group of diseases due to infection 143 patients were seen. It is most interesting to note that not one case of diphtheria occurred. A patient with leprosy (male) was first considered to be luetic; the disease was contracted in Africa. There were twelve cases of chickenpox and eight of mumps. One case each of mumps and chickenpox was an adult aged seventy (male) and an adult aged thirty (woman) respectively. Of the 21 patients with pulmonary tuberculosis all were adults except a boy of sixteen and a girl of nineteen. Seven tuberculous patients are in bed at home at the time of writing and are unable to obtain admission to a sanatorium. One of the six cases of syphilis was a man who had "laryngitis" which did not respond to three weeks' treatment; another was a woman with a tonsillar abscess which was resistant to treatment. Only two of the eighteen patients with scarlet fever were sent to an isolation hospital. Of the ten patients with gonorrhœa, eight were men (three married) and two were women (both married). Only one of the ten cases of whooping-cough was an adult, all the eighteen cases of rubella were adults and all the seventeen cases of measles were children. One of the two patients with meningitis died. Pneumonia accounted for twelve, malaria for one, and vulvo-vaginitis for three cases respectively.

AFFECTIONS OF THE SKIN

Perhaps a greater number than usual of skin conditions were seen because one afternoon surgery each week was devoted to them. A total of 415 patients were treated. In an industrial district dermatitis is met with in many forms and disguises. The six cases of tinea cruris were most extensive and had been "going strong" for some months when advice was sought, there were four men and two women, one of the men had been discharged with it from the Forces after fifteen years' service, all the cases were clear in two months. A woman with an epithelioma

of the skin of the upper arm of many years standing, and which she said had developed on a "birthmark," was sent for a biopsy and subsequently successfully treated with X-rays

Of the cases of contact dermatitis, one was due to the spectacle frame, another to an antiseptic used by a veterinary surgeon, several were caused by hair dye and cosmetics, two were allergic to nickel suspender parts, one was caused by an earphone (telephonist), and two were abnormally sensitive to soap flakes. Of the twenty-nine patients with septic conditions of fingers and hands all but two were men, and most of them had been previously treated at their place of work. The liquid used for "petrol" lighters was responsible for two of the eighteen cases of burns and scalds and both were extensive and caused some anxiety

It is interesting, in view of the many articles published on the treatment of impetigo contagiosa, that all the twenty-four cases cleared within seven days of treatment with 5 per cent sulphathiazole in a water-soluble base. All but two of the patients with scabies were treated at a Municipal Cleansing Centre, and one health insurance patient who was cured of her ailment at the Centre, returned afterwards and asked to change her practitioner, and did so, as she said that she had never been so insulted as by being sent there!

Six cases of infantile eczema were seen and relieved, as were twenty-two adults with eczema. Fortunately, although having a fair number of "chronics," only two bed sores occurred. Not one of the four patients with acne vulgaris was much helped by any form of treatment, but three of the four cases of lupus vulgaris were completely relieved, as were also all the ten cases of seborrhœic dermatitis. Urticaria (26 cases) is frequently a troublesome condition, varicose ulcers (15 cases) were cured in those patients who submitted to elevation, rest, lotions and injection of the causal vein. Although two of the eight patients with erysipelas were seriously ill, they were all completely cured in a short time with sulphonamides, local treatment and analgesics.

Some other conditions seen were, epidermophyton infection of feet (16), dandruff (10), corns (10), bee and wasp stings and insect bites (7), warts (6), neurodermatitis (6), cheilopompholyx (4), chilblains (12), pruritus ani (6), ringworm (10), disease of nails (6), excoriated buttocks in babies (3), boils (4), carbuncles (8), rosacea (4), pediculosis (4), purpura (2), pityriasis rosea (4), moles (3), naevi (2), angio-neurotic œdema (4), sycosis barbæ (2), drug rash (2), hyperidrosis (4), ichthyosis (2), Bockhart's impetigo (2), serum sickness (2) and perlèche (5).

DISEASES OF THE EAR, NOSE, MOUTH AND THROAT

In all, 310 cases were treated, including fifteen of otitis media, only one of which required paracentesis of the tympanic membrane. One of the four patients with quinsy needed an incision, and all of the fourteen cases of sinusitis were treated successfully without puncture. Only one child has been seen with thrush.

Many cases of enlarged unhealthy tonsils and adenoids in children appeared to improve considerably with breathing exercises, sulphacetamide "paint," vitamins, tonics and sulphanilamide lozenges, this appears to be important, owing to the long waiting lists for "T's and A's." The use of the sulphonamides for the thirty-nine cases of tonsillitis was a considerable advance over other types of treatment.

Two of the three patients with paroxysmal rhinorrhœa were kept free from all symptoms for a period of six months by means of injections of the suitable substances which were indicated from the results of skin tests. It was found that massive dosage of nicotinamide and vitamin C quickly cleared up the three cases of Vincent's angina.

Pharyngitis (18), upper respiratory catarrh (36), rhinitis (12), hay fever (8), curvature of nose (6), gingivitis (8), otitis externa (8), stomatitis (8), ceruminous obstruction (54), were some of the other cases encountered. Not one case of acute mastoiditis was seen, but two adults with running ears of many years' duration were sent for operation. In all, twenty-two children had their tonsils and adenoids removed. Menière's disease, hæmatoma auris, pyorrhœa alveolaris, polypus of nose and ear were each seen twice.

DISEASES OF WOMEN

In all, 222 cases were treated, including 30 for abortion. Six embryos and fetuses were obtained and are now in formalin. Three patients were sent to hospital with hæmoglobin estimations in the range of 24 to 30 per cent.

One woman aged twenty-four with uterine hæmorrhage, which persisted after a Cæsarean operation two years previously, had been seen at various times by three gynæcologists, bleeding was controlled by injections of progesterone and ethisterone by mouth, and it was suggested that the cause of the trouble was the use of silk for suturing the uterus. Two married patients, aged twenty-seven and thirty respectively, were diagnosed after biopsy as metropathia hæmorrhagica, both were advised by a gynæcologist to undergo hysterectomy. One, who was childless, had hysterectomy and became strong and well, the other, with one child aged seven, decided against the operation and was treated at home and subsequently returned to work, but she has had two short relapses. Under the heading of menopausal conditions are included some patients in the thirty-two to seventy-four age period, who complained of symptoms of the climacteric and were considerably relieved by treatment.

All the leucorrhœa and vaginal discharge cases (22) were swabbed and two had trichomonas infection (cases of gonorrhœa are not included here). Of the fourteen patients complaining of pruritus vulvæ, one was due to threadworms, three to contraceptives, one to cervical erosion and some to the menopause.

All the four young women who came for advice on sterility and the four with frigidity were sent to a special clinic. It is a source of gratification that all of the twelve women who had sickness and vomiting of pregnancy were relieved. Albuminuria of pregnancy was encountered twice, and one case of menorrhagia of puberty in a girl of thirteen responded at once to injections of progesterone. Of nine patients with mastitis after pregnancy, three needed hospitalization and incision. One of the six cases of dyspareunia was due to an intact hymen, the only patient with inversion of the uterus was a young woman having her second child, her firstborn being a "Cæsar", the placenta came on its own and with its delivery the uterus inverted.

Some other conditions were dysmenorrhœa (23), retroversion (8), salpingo-

oophoritis (3), prolapse of uterus (6), uterine hæmorrhage (10), fibroids (3), cervical erosion (3), cystocele (3), cancer (bilateral) of ovaries (1), amenorrhœa (9)

METABOLIC AND DEFICIENCY DISEASES

Two men and one young woman with ariboflavinosis were "classical" cases and quickly responded to treatment. Of the twelve cases of diabetes mellitus, two were elderly women, aged seventy-four and seventy-two, and they were stabilized in hospital. All the nineteen patients with obesity were women, they were given a diet sheet, three had thyroid medication, and all were weighed regularly and expected to lose one pound a week, but only four responded satisfactorily.

DISEASES OF THE LOCOMOTOR SYSTEM

A total of 337 cases included one case of osteomalacia, a woman aged sixty-eight who complained of backache, which was not relieved by conservative treatment, an X-ray of the spine clinched the diagnosis. All the fractures (34) were treated at the local fracture clinic. Among the types of fracture seen were two "march fractures," a spontaneous fracture of the humerus (sarcoma), six of the big toe and other toes due to falling objects at work, three of the skull, two Pott's, three carpal scaphoids, two greensticks, and six fractures of the ribs.

About one hundred and seventy cases of rheumatism in all its aspects were seen. It is most interesting to note that experience showed that in lumbago, fibrositis, sprains and allied conditions, the patient was returned to work or activity within twenty-four hours or so by the use of injections of procaine and medication, whereas physiotherapy entailed days or weeks of treatment, loss of work and a doubtful end-result in many cases. It is hoped to publish elsewhere an account of this method.

Four of the five cases of ganglion were successfully treated by aspiration and injection of a sclerosing liquid. Some other cases were sprains (57), claw foot (5), Dupuytren's contracture (4), genu valgum (3), gout (7), internal derangement of the knee (2), metatarsalgia (3), pes planus (20), scoliosis (6), tenosynovitis (3), and trigger finger (1).

DISEASES OF THE DIGESTIVE TRACT

In all, 285 cases were seen, including one of intestinal obstruction in a man of seventy-four, due to a strangulated umbilical hernia. Peptic ulcer (28), dyspepsia and gastritis (50), aerophagy (18), diarrhœa (31), constipation (25), and intestinal colic (21), are encountered at almost every surgery, as is also some form of "nerves." There were two night-calls for perforation, both true bills, and there were eight cases of appendicitis (five operated upon). A male first-born child with congenital pyloric stenosis was one month old and did well after operation. One of the six patients with hæmatemesis had two bouts during the year; he was a bus driver. Gall-bladder trouble accounted for six, colitis four, and round worms two cases, respectively. It seems that the newer remedies for threadworms (gentian violet, diphenan) are more effective than the older ones, provided parent and child are treated at one and the same time, and provided also that nails are cut short, hands

washed before eating, gloves worn in bed and ointment, such as dilute ammoniated mercury ointment, is applied around the anus, and an enema (e.g. quassia) given at the start and at the end of treatment. In this way all the seventeen cases treated were cured, with only one relapse.

DISEASES OF THE RESPIRATORY TRACT

Three hundred and one cases were treated, including influenza (102), catarrh (62), and the common cold (31). One of the twelve patients with asthma visited my house regularly on Sunday mornings, with an attack, to have an injection of adrenaline, until he was forbidden cheese, which he regularly had for supper on Saturdays only. Four cases of hæmoptysis were seen but only one, after investigation, was diagnosed as tuberculous. In this connexion it is interesting and instructive to note that of the twenty-one cases of pulmonary tuberculosis only two had any abnormal physical signs. Some other cases were, bronchitis, acute and chronic (37), congestion of the lungs (16), laryngitis (15), pleurisy (4) and tracheitis (22).

DISEASES OF THE BLOOD AND CARDIOVASCULAR SYSTEM

In all, 271 cases were treated, the sole case of hæmophilia was frequently in trouble. Apparently he is most interested in his condition and has had, without much apparent result, almost every kind of treatment, orthodox and unorthodox. Five of the twenty-two patients with hypertension had a systolic blood pressure higher than 240 mm of mercury. Three of the cases of pernicious anæmia included the whole of one family, mother, father and daughter. The ten patients with congestive heart failure include a man who has two injections of mersalyl a week, a young girl of seventeen who is "tapped" almost weekly and from whom about fourteen pints of fluid are obtained each time, and a man who has had two coronary thromboses (confirmed by electrocardiogram). Most of the thirty-two cases of tachycardia presented some difficulty, as a cause could not be found for the condition. Of the fifty-eight patients with varicose veins, at least four had been previously treated by operation and injection without much relief. Agranulocytosis accounted for two cases. Some other cases were, angina pectoris (6), arteriosclerosis (10), auricular fibrillation (14), bacterial endocarditis (1), cerebral hæmorrhage and embolism (9), epistaxis (6), myocardial insufficiency (18), paroxysmal dyspnoea (9), thrombophlebitis (6) and valvular disease (17).

DISEASES OF THE NERVOUS SYSTEM

The three cases of impotence in this group, which totalled 180, were young married men with children. Eleven of the twelve sufferers from migraine were women and all were considerably helped and relieved by ergotamine tartrate. Neurasthenia accounted for eighty-two cases, eleven were seen by a psychiatrist, and four had in-patient treatment at a mental hospital in which only one stayed for the whole course. Only four of the twenty-six people who complained of insomnia needed help after a few days' medication. The sole case of "amyotrophic lateral sclerosis" had an interesting sequel —

A labourer aged sixty-seven and weighing 90 lb was sent to hospital, investigated, diagnosed as above, and sent to the Infirmary, and after several weeks was sent home.

Subsequently a blood count indicated a macrocytic hyperchromic anæmia and injections of liver extract were then given, with a mixture of phenobarbitone soluble $\frac{1}{2}$ a grain, vitamin B 2 mgm, vitamin C 50 mgm, with water to half an ounce, thrice daily for a few weeks. Improvement was rapid, and six months later the man walked to the surgery and weighed 126 lb.

Some other cases were disseminated sclerosis (3), epilepsy (12), hysteria (4), neuralgia (14), paralysis agitans (6), Raynaud's disease (1), and vaso-vagal attacks (3).

DISEASES OF THE GENITO-URINARY SYSTEM

Included in this group of 101 cases are ten of enuresis, of which eight were men. A woman with polycystic kidney, also suffered from hypertension and pulmonary tuberculosis. One of the six patients with hæmaturia was ninety-three years old, a woman, who recovered and again undertook all her household duties, after massive doses of vitamin C. Some other cases were bacilluria (22), cystitis (12), frequency of micturition (21), incontinence (all women) (6), renal calculus (1), aberrant renal vessel (1), nephritis (2), pyelitis (7), retention of urine (1), enlarged prostate (3), and carcinoma of prostate (1).

DISEASES OF THE EYES

In this group (in all 155 cases) thirty patients with conjunctivitis were seen. Of the forty-one foreign bodies removed, twenty were from the cornea. One child was seen with a punctum absent from the lower lid. Errors of refraction (25), hordeolum (12), colour blindness (2), blepharitis (12), cataract (4), corneal ulcers (2), meibomian cysts (4), episcleritis (1), herpes ophthalmicus (1), trichiasis (2), obstruction of canniculus (2), were some of the other cases.

COMMENTS

To keep a record of, and to analyse, these activities did not entail much extra work. A series of graphs were marked daily. A special system was used to enter in a day book essential details of each patient seen. A book was used for all pathological findings, and the usual dispensing book was kept. Weekly and monthly analyses were made.

However, it must be stressed that a practitioner's work entails more than is recorded or indicated in the foregoing. The cards of panel patients have to be "written up," records of private patients have to be kept, and there is the business of running a practice. Then there are many unrecorded and unrecordable jobs, such as interviewing relatives of sick folk, often at the practitioner's private house, inquiries and advice on the telephone, examination of boys for a cadet corps, and visits from patients for advice on varied non-medical matters.

The figures may be all the more interesting to many people in view of the interest taken in social medicine, and in the recent White Paper dealing with the medical and health services, for they show that practitioners are busy and are doing plenty of work. An average of sixty people were seen and sixty-six prescriptions, certificates and letters written every working day, these figures give much food for thought and possible scope for analysis.

CHILD HEALTH

XIV—THE DEAF CHILD

By A H GALE, D M, D P H

Ministry of Education

SEVERE deafness in children is, fortunately, so uncommon that any individual general practitioner is unlikely to see more than one or two cases in a lifetime. He may therefore find himself at a loss as to how to deal with such cases, and so this article is written largely from the practical point of view. Clearly some form of classification is necessary, because the term "deafness" may be taken to cover any degree of defect from complete deaf-mutism to a defect so slight that it can be detected only by special tests. Many different terms have been used to describe different degrees of deafness but the method which is now in fairly general use is that suggested by the Board of Education Committee (1938)

CLASSIFICATION

They suggested the following educational grades —

Grade I —Children with defective hearing who can, nevertheless, without special arrangements of any kind, obtain proper benefit from the education provided in an ordinary school—elementary, secondary or technical

Grade II —Children whose hearing is defective to such a degree that they require for their education special arrangements or facilities, but not the educational methods used for deaf children without naturally acquired speech or language. These facilities range from a favourable position in the ordinary school classroom to attendance at a special class or school

Grade IIA. Those children within grade II who can make satisfactory progress in ordinary classes in ordinary schools provided they are given some help, whether by way of favourable position in class, by individual hearing aids, or by tuition in lip-reading

Grade IIB. Those children within grade II who, even with the help of favourable position in the class, individual hearing aids or tuition in lip-reading, fail to make satisfactory progress in ordinary classes in ordinary schools

Grade III —Children whose hearing is so defective and whose speech and language are so little developed that they require education by methods used for deaf children without naturally acquired speech or language. This grade includes the totally deaf

It will be noticed that this classification does not depend only upon the degree of hearing defect but on other factors also. It has been found in practice that, although the degree of hearing defect is the most important single factor in determining what method of education is desirable, other important factors are intelligence, age of onset of deafness, the degree to which speech and understanding

of speech have developed and ability in lip-reading. An intelligent child who has a severe hearing defect may make good progress in an ordinary school. I have even been told of one child said to be totally deaf who made good progress in an ordinary secondary school. On the other hand, an unintelligent child with a less severe defect may require specialized methods of education to make any progress at all. For all these reasons the information as to a child's educability to be gained from an assessment of his hearing capacity is limited, and the method of trial and error may have to be used in selecting the appropriate educational treatment.

CAUSES

Except for a few cases due to injury, deafness is due either to genetic causes or to infection. The latter may be congenital or acquired. Generally speaking, the genetic cases have a severe degree of deafness, although modern methods of testing with electrical apparatus have shown that many of the children who would formerly have been described as totally deaf have islands of hearing. These modern methods have also made possible the investigation of an interesting group of cases of "high note" deafness to which further reference will be made. It is probably true to say, however, that all cases of deafness due to genetic causes will come within grade III or grade IIB. Deafness due to infections may on the other hand be of any degree of severity. On the whole, those due to *cerebro-spinal meningitis* are the most severe, whereas those due to *otitis media* are seldom complete, and may be so slight as to escape detection altogether unless a special search is made for them.

Congenital syphilis is usually given a prominent place among the causes of deafness in childhood, but in a small investigation recently undertaken (Gale, 1944) the number of cases definitely ascribed to this cause was so small as to be not worth recording under a separate heading. The actual number was four out of 730 children admitted to four schools for the deaf between 1938 and 1944. In this investigation about half the cases were ascribed to genetic causes and of the remaining half about one-third were ascribed to *otitis media*, one-third to *cerebro-spinal meningitis* and the other third was a heterogeneous group due to various infections, congenital syphilis, trauma and unknown causes. It should be emphasized that these figures must be treated with considerable caution because it is often difficult to get reliable information about the cause of deafness a few years after its onset. It would be of great value to the school authorities if practitioners who have deaf children as their patients would do their best to ensure that any medical information of value is transmitted to the school medical officer of the Local Education Authority which sends the child to a school for the deaf.

DIAGNOSIS

The diagnosis of severe deafness in a young child is often difficult, and even with older children of poor intelligence, it is often extremely difficult to decide how far symptoms are due to deafness and how far they are due to poor intelligence. Perhaps the best way to approach the problem is to consider first the child who is born deaf, and secondly the child who acquires severe deafness at an age when his speech has developed.

In her detailed study of young deaf children, Mrs Ewing (1943) showed that the totally deaf baby nearly always develops babbling sounds in exactly the same way as does his hearing brother, and that it is only at the age of about eighteen months when the babbling of the normal child begins to develop into coherent speech that the babbling of the deaf child begins to retrogress. She also found that those children who had some islands of hearing showed normal motor development, but totally deaf children showed some slight retardation. Both types showed more or less normal development of adaptive behaviour. These facts are of importance in diagnosis because, on the whole, the early landmarks of development tend to be reached at the same age in deaf as in normal children, and any great delay in their attainment raises the question of mental subnormality.

The application of *hearing tests* to very young children is a difficult matter but the Ewings (1938, 1944, 1945) have described a technique for the testing of babies. Briefly this consists of finding out by means of play whether the child can hear —

- (1) Percussion sounds, such as a drum, a loud bell, a triangle
- (2) Meaningful noises, such as the crackling of paper, chinking of feeding bottles, tap at the door, footsteps approaching
- (3) Voice in "talking" to the child
- (4) Speech when he is old enough, e.g., child's own name, easy commands "Come to Mummy," "Give one to——"
- (5) If obtainable, pitch pipes covering a range of notes from about 200 vibrations to 2,000 vibrations a second

Simple speech tests are suitable for most children of fifteen months and over. For details of a simple method of testing very young children see Ewing (1945).

The most common mistake made in observing the deaf child is to assume that he hears when in fact he either feels vibration or a movement of air. For example he may turn his eyes when the observer claps his hands behind his head because he feels the movement of air, or he may turn his head when somebody walks across the room because he feels the vibration. It must be remembered, too, that the child may have islands of hearing so that either high-pitched or low-pitched sounds of relatively low intensity may be heard although the general level of hearing is inadequate for the development of speech.

The child who acquires deafness may acquire it suddenly—usually as a result of cerebro-spinal meningitis—or he may go deaf slowly as a result of progressive middle-ear disease. If he becomes deaf before speech has developed his problems will be similar to those of the child who has congenital deafness, but once he has developed speech and, even more important, language, which includes understanding of the spoken and written word, his problems are different. Speech becomes his natural medium and, although he may lose a great deal of facility in it, particularly if he is allowed to go without proper teaching for any length of time, he is always at a great advantage compared with the congenitally deaf child. The psychological effects of sudden deafness are naturally profound, and it often happens that a child so afflicted ceases to speak, but this does not mean that with skilled treatment his speech will not recover. It is an urgent matter to secure skilled teaching for a child who acquires severe deafness, because he is losing something every day.

HEARING TESTS

Mention has been made incidentally of certain hearing tests, but it would be impossible to discuss this large subject in detail here. It may, however, be useful to mention certain general principles and some common mistakes which are made in administering, or in assessing, the results of hearing tests. The principal point to remember are—

- (1) That normal hearing is many times more sensitive than it need be for most of the ordinary purposes of daily life. A considerable reduction of acuity may easily pass unnoticed, and is in fact compatible with normal behaviour.
- (2) Deafness is seldom complete and islands of hearing for sounds of a certain pitch may exist in children who have very little power of recognizing speech.
- (3) Some facility in lip-reading, or rather in speech reading, may be rapidly acquired by an intelligent child even without formal instruction.
- (4) Deaf children are particularly sensitive to vibration or air movements and may appear to hear a sound when they are really perceiving vibration or a movement.
- (5) It is extremely difficult to control the intensity of speech sounds and an observer tends to raise his voice when there is background noise. A familiar example is the penetrating and often embarrassing loudness of a remark made during a general silence at the dinner table.

For these reasons the results of tests which depend upon speech and which are conducted in an ordinary room are only approximate. They may be useful in the preliminary investigation of a case but they should be supplemented by audiometer tests, in which the pitch and intensity of the test sound is controllable and measurable. Such tests are outside the scope of this article and information on them is contained in the Ewings's book (1938) and in the Report of the Committee of the Board of Education (1938). A type of audiometer known as a gramophone audiometer has been devised for the group-testing of children's hearing, but this instrument is perhaps more useful for picking out those children who need investigation and medical treatment than for finding children who suffer from severe deafness.

RARE CONDITIONS SIMULATING DEAFNESS

Reference has already been made to the difficulty which sometimes arises in distinguishing between the deaf child and the mentally subnormal child. This is undoubtedly the most common cause of difficulty in differential diagnosis, but there are rare cases of children who are of normal intelligence, who can hear and who cannot speak intelligibly. The causes of this condition of congenital auditory imperception are obscure and there is doubt as to the best methods of treating it but most of the children seem to derive benefit from educational treatment in school for the deaf. Worster-Drought (1943) has recently discussed the relationship of this condition to deafness and speech defects.

One form of deafness—deafness to high notes—may give rise to special difficulties because the child may appear to have normal hearing by rough tests, although his hearing for high notes is so defective that his speech and understanding of language are grossly affected. Such children may easily be regarded as mentally defective (Sheridan, 1944). Any child over seven who is very backward and has a speech defect—particularly a defect involving S, Sh—should be examined with a pure tone audiometer.

EDUCATION

When the presumptive diagnosis of severe deafness has been made, the problems of treatment and education arise. This article is not concerned with the details of purely medical treatment, but it is assumed that whatever a competent otologist can do to improve the deafness will be done. There will remain, however, a substantial number of children for whom little can be done to improve the deafness but much by way of education.

The Education Act 1944 makes some important changes in the law relating to deaf children. Under this Act it is the duty of the Local Education Authority to provide education for a deaf child from the age of two, if the parents desire it. The age at which education becomes compulsory is five. In the regulations made under the Act, deaf pupils are defined as "pupils who have no hearing or whose hearing is so defective that they require education by methods used for deaf pupils without naturally acquired speech or language." These deaf children must be educated in a special school unless the Minister of Education determines otherwise. Under the old Act and Regulations no separate class of partially deaf pupils was recognized, but under the new Regulations partially deaf pupils are defined as "pupils whose hearing is so defective that they require for their education special arrangements or facilities but not all the educational methods used for deaf pupils." It is contemplated that some of these children will need education in special schools but that others may make good progress in ordinary schools, if they are given a favourable position in the classroom, hearing aids if necessary, and tuition in lip-reading. It will be noted that the term "deaf" corresponds with grade III of the classification previously given and that "partially deaf" corresponds with grade IIA and B, grade IIA being those children who can make satisfactory progress in an ordinary school with special help and grade IIB being those who need education in a special school.

To determine the best type of education for a deaf child may be no easy matter and the best method of approach is for the general practitioner to consult with the school medical officer of the Local Education Authority. The school medical officer may be able, in doubtful cases, to arrange for consultation with an experienced teacher of the deaf. Often the only satisfactory way of deciding whether a child should be in a school for the deaf or not is to send him to one for a trial period, for those who have most experience are least ready to make hasty judgments as to the mental capacity of deaf children. The most difficult cases to decide are those in which there is some degree of deafness associated with some degree of intellectual incapacity. Franklin (1938) has suggested methods for utilizing the sense of vibration for teaching young deaf children.

Schooling for the deaf child—Once it is decided that any child over the age of two is so deaf as to need education, or at any rate a trial, in a special school it will nearly always be desirable to set in train the application for his admission. In the ordinary way the arrangements will be made by the Local Education Authority but a few parents may wish to send their child to a private school and pay fees. The private schools are few in number and are, generally speaking, much smaller than those which receive children mainly through Local Education Authorities.

For the names of private schools it is well to consult the National Institute for the Deaf, Gower Street, London, W C 1 (At the present time, owing to war conditions, there is a shortage of places in special schools for the deaf and some delay in admissions is inevitable. It is hoped that this state of affairs will be remedied as soon as possible after the war.)

A good deal can be done at home by the mother of a young deaf child who is either too young for admission to a special school or whose admission is delayed for some reason, and an excellent little booklet of advice has been prepared by the Ewings. This may be obtained on application to Dr A W G Ewing, Department of Education of the Deaf, The University, Manchester. A useful book of general advice called "All about the Deaf" is published by the National Institute for the Deaf.

CONCLUSIONS

The principal points made in this article are —

(1) The deaf child usually develops more or less normally up to the age of about eighteen months, when babbling should develop into speech.

(2) The diagnosis of severe deafness is often difficult and may require the assistance of those with special experience of deaf children. Deafness should always be excluded in a child whose speech is seriously defective, even though he seems to hear certain sounds.

(3) The mother can do much to prepare the way for special education of the deaf child, but special educational methods are essential and these should be started as soon as possible after the age of two. Training in lip-reading and the encouragement of the use of the voice should begin even earlier.

(4) Unless the parent wishes to send his child to a private school and pay fees, it is the province of the Local Education Authority to arrange for the special educational treatment of a deaf child over the age of two. Up to the age of five it is permissive for the parent to have his child educated, but after that age it is a legal obligation.

Thanks for help in the preparation of this article are due to Dr J E Underwood, J Lumsden, H M I, Dr A W G Ewing, and Mrs Ewing, O B E.

References

- Board of Education (1938) "Report of the Committee of Inquiry into Problems Relating to Children with Defective Hearing," pp 48, 35.
 Ewing, Irene R, and Ewing, A W G (1938) "The Handicap of Deafness," London pp 85, 64.
 — (1943) *J Laryng Otol*, 58, 4.
 — (1944) *Ibid*, 59, 309.
 — (1945) "Mother and Child," pp 16, 17.
 Franklin, P (1938) *The Practitioner*, 141, 613.
 Gale, A H (1944) *Mntly Bull Min Hlth*, 4, 164.
 Sheridan, Mary D (1944) *Brit med J*, 2, 272.
 Worster-Drought, C (1943) *Med Pr Cir*, 210, 411.

NOTES AND QUERIES

STREPTOCOCCAL INFECTION AND SCARLET FEVER

QUESTION (from a subscriber in London) — What evidence is there for and against the opinion that hæmolytic streptococcal infection of the fauces, unassociated with a scarlatiniform rash, commonly produces a disease which, apart from the absence of rash and effects of same, is identical with scarlet fever?

REPLY — There is clinical, bacteriological and epidemiological evidence that scarlet fever is, except for its rash, the same disease as tonsillo-pharyngitis due to hæmolytic streptococci. In every outbreak of scarlet fever a proportion of those infected suffer from a simple tonsillo-pharyngitis due to the same type of streptococcus as that responsible for the cases of scarlet fever. The course of the disease, its duration and complications, are the same, differences in degree but not in kind occurring. The presence of the rash is determined by two factors. On the one hand there is the susceptibility of the skin to the erythrogenic toxin, determinable by the Dick test. On the other hand there is the capacity of the prevalent streptococcus to produce erythrogenic toxin. The thirty or more types of hæmolytic streptococci vary considerably in this respect and therefore in their ability to cause scarlet fever; Hamburger *et al* (*J Amer. med. Ass.*, 1944, 124, 564) found that type 3 streptococci caused scarlet fever in 46.6 per cent. of their cases of tonsillo-pharyngitis, whilst type 19 did so in 16.5 per cent. and type 1 in 4.3 per cent. Types 6 and 36 did not cause scarlet fever. It follows, that outbreaks of tonsillo-pharyngitis may occur without cases of scarlet fever. Comparison should be made between tonsillo-pharyngitis and scarlet fever due to the same type or strain of streptococcus for the identity of the two forms to be apparent.

M MITMAN, M.D., F.R.C.P., D.P.H.

VAGINAL ACIDITY AND STERILITY

QUESTION (from a subscriber in Surrey) — What is the significance of a high vaginal acidity in a patient who is sterile? A patient in her late thirties, married for six years, is desperately anxious to have a child. I have just received a report to the effect that the pH of a vaginal wash-out is 3.5. I should be grateful for any suggestions as to the significance of this, and the best means of dealing with it.

REPLY — High vaginal acidity may be of no significance, for example, if insemination into the cervix is direct or a large amount of cervical secretion is poured out during intercourse. It is necessary, however, before deciding the importance of this factor, to examine a post-coital

specimen of cervical mucus, obtained by suction, for the presence of live spermatozoa. If these are actively motile up to several hours after intercourse, the high vaginal acidity is of no significance. If the spermatozoa from the cervix are all non-motile, yet motile in a condom specimen, vaginal douching with a solution of bicarbonate of soda, 60 grains to a pint, is advocated an hour or two before sexual intercourse, to counteract vaginal acidity and thus preserve sperm in order that they may live to find their way into the cervix.

M. MOORE WHITE, M.D., F.R.C.S., M.R.C.O.G.

THE AROMATIC AMIDINES

QUESTION (from a subscriber in the Navy) — What is known to date of the pharmacology and therapeutics of the aromatic diamidines? In what clinical conditions have they been tried? Has any definite information been published on the best type of these drugs to use, their dosage, and method of administration?

REPLY — The most important aromatic amidines are stilbamidine, propamidine and pentamidine. These compounds have been found to be effective in the treatment of African trypanosomiasis and Indian and Sudanese kala-azar and they also have limited activity in malaria. In trypanosomiasis, pentamidine, the most frequently used drug of the group in this disease, is only effective in early and relatively mild cases. In kala-azar the drugs are probably more effective than antimony compounds. In these diseases the amidines are given by intravenous or intramuscular injection, chiefly by the former route. The dosage is 0.5 to 2.0 mgm./kgm. body weight daily for ten or more days, and the drug must be given very slowly into the vein to avoid a sharp transient fall of blood pressure, which is mainly due to vasodilatation. Apart from the lowered blood pressure there may be intense itching, but generally, toxic effects are few and not serious. Propamidine has also been used as an antibacterial agent by direct application to infected wounds and burns. It is made up either in a jelly or in lanette wax (0.1 per cent. propamidine) and is particularly active against hæmolytic streptococci, less so against staphylococci, and has no action on proteus or pyocyanea. This antibacterial action is not inhibited by pus or by *p*-aminobenzoic acid (c.f. sulphonamides) 0.1 per cent. propamidine is said not to inhibit phagocytosis nor to damage granulation tissue, but there is no doubt that this substance is more harmful to tissues than sulphonamides or penicillin. Propamidine is probably not an effective antibacterial agent when given intravenously.

C. A. KEELE, M.D., M.R.C.P.

PRACTICAL NOTES

THE USE OF LOCAL PENICILLIN IN
OPHTHALMIA NEONATORUM

FOLLOWING an earlier report on the use of local penicillin therapy in a series of cases of ophthalmia neonatorum, A Sorsby (*British Medical Journal*, June 30, 1945, **I**, 903) records the results obtained in a further series of thirty-eight cases. The method adopted was as follows—A swab for smear or culture was taken on admission and then the eye irrigated with half-normal saline at room temperature. A drop of adrenaline, 1 in 1,000, was instilled, and a scraping taken for examination, atropine being instilled if the cornea was involved. Accumulated pus was wiped away, one drop of penicillin in a concentration of 2,500 units per c cm instilled, and the baby returned to its cot. The instillation of penicillin was continued every five minutes until all discharge had disappeared, then at half-hourly intervals, and finally, hourly for twelve hours and two-hourly for a further twenty-four hours. The five-minute applications usually occupy half an hour to three hours (6 to 30 applications), the half-hourly instillations about six to twelve hours. No irrigation is needed, any thin mucoid discharge being ignored or, if clinging to the lids, wiped away with moist pledglets of cotton-wool. In twenty-five cases in which this method was carried out only two failed to respond, five required a second course, and in the remaining eighteen clinical cure was obtained within an average of just under ten hours. The remaining thirteen cases of the thirty-eight of the series were treated with penicillin drops at one-hourly intervals for six hours, then two-hourly for twenty-four hours, and finally at three-hourly intervals. All the infants responded well but in one case relapse occurred after twenty-four hours and in another after a lapse of five days. Both these cases cleared up after a course of sulphamezathine.

INTRAVENOUS ALIMENTATION WITH
PROTEIN

THE increasing use of the intravenous administration of protein lends interest to a study of forty-nine surgical patients to whom two hundred consecutive injections of a protein digest were given by C S White and J J Weinstein (*Surgery, Gynecology and Obstetrics*, March 1945, **80**, 313). The protein digest solution, which was prepared from an enzymatic digest of a mammalian protein, is prepared by a method that removes all toxic constituents, maintains the sterility of the mixture, and yields a stable, heat sterilized, pyrogen-free solution with a pH of approximately 6.5. At least 50 per cent of the nitrogen is present as free α -amino nitrogen, and the solution is free of undigested

proteins and proteoses. The average amount given in each injection was approximately a litre (equivalent to 60 gm protein), the total amount individual patients received ranging from 500 c cm to 21 litres. The average rate of injection was approximately 10.5 c cm per minute. Only seven reactions were encountered in two hundred consecutive injections. Two of the reactions occurred in one patient and consisted of flushing of the face, a feeling of warmth, nausea and vomiting, this type of reaction attributed to substances in the digest that cause vascular reactions. The other five reactions consisting of chills and slight pyrexia, are attributed to pyrogens present in the tube and needles used for the injection. In no case was acute thrombophlebitis observed due to the injection. Many of the patients to whom the digest was given were seriously ill, and by this method it was possible to ensure an adequate intake of protein. Even after relatively minor surgical procedures, such as hernioplasties, the authors found a negative protein balance post-operatively, the average protein deficit for the first seven post-operative days being 70.83 gm nitrogen, or 442.68 gm protein. In seriously ill patients the deficit must be even greater, and, as the intake by mouth is restricted, intravenous alimentation provides a safe and reliable method of supplying protein. By the addition of glucose, vitamins and inorganic salts to the solution, it is suggested that the patient's nutrition might be even better maintained.

SULPHAGUANIDINE, SULPHATHIAZOLE AND SUPRARENAL CORTEX
EXTRACT IN THE TREATMENT OF
CHOLERA

A REPORT on observations in the cholera war of the Chittaranjan Hospital, Calcutta, by S C Lahiri (*Journal of the Indian Medical Association*, March 1945, **14**, 113) covers a period of four months from June to October 1944, during which time 315 cases were admitted. In 114 of these cases sulphaguanidine was given as an intestinal antiseptic, in 2 sulphathiazole and in the remainder calomel was used. All patients were given saline transfusion and 100 to 200 c cm of 25 per cent glucose solution daily, by intravenous route, also atropine sulphate 1/200 to 1/100 grain subcutaneously, once or twice daily, unless contraindicated. There were 76 deaths: 17 in the sulphaguanidine treated group (four after taking only 2 gm or less), 7 in the sulphathiazole treated group and 52 in the calomel treated group. The dosage of sulphaguanidine was originally 1 gm initial dose, followed by the same dose at two-hourly intervals for two more doses, and then at four

hourly intervals until the patient had received 5 gm in twenty-four hours. Later the dosage was slightly increased, the initial dose being 2 gm and the following doses and intervals the same as before, the total dose in twenty-four hours being 6 to 7 gm. The majority did not receive more than 10 gm. in two days, a few resistant cases had a total of 15 gm. in three days. The dosage of sulphathiazole was 1 gm. on admission followed by the same dose at two-hourly intervals for two doses and then at four-hourly intervals until the patient had received 5 to 6 gm. in twenty-four hours. Total dosage 10 gm. in two days. In ten severe cases extract of suprarenal cortex was given intravenously, in dosage of 2 c.cm. eucortone mixed with 100 c.c.m. of 25 per cent glucose solution, generally after saline transfusion, the same dose being repeated at six-hourly intervals according to necessity. In this group of ten patients there were two deaths after receiving only one dose of 2 c.c.m., of the remainder, one received a total dose of 8 c.c.m., four 4 c.c.m., and three 2 c.c.m. Restoration and maintenance of the radial pulse was noted in these patients, but the series was too small for any definite conclusions. Sulphaguanidine seemed to be an effective remedy in the majority of the treated cases the stools changed to yellow or greenish colour after a total dose of 5 to 6 gm. or less. In twenty cases a total dose of 6 gm. was required to produce this change, and in one case as much as 14 gm was necessary. As regards complications with sulphaguanidine, in one case fatal hæmorrhage from the gastro-intestinal tract occurred after 10 gm. of the drug had been administered, and after a total dose of this amount a slightly reddish tinge of the stool was noticed in some other cases, this cleared up on stoppage of the drug. In a few cases there was intestinal colic, and vomiting occurred in some cases after a total dose of 10 gm. Both these symptoms cleared when the drug was stopped. It is stated that the beneficial effect of sulphaguanidine is more marked in the early stage or milder cases of the disease, before irreparable damage has been caused, than in the late stage.

EMETINE IN THE TREATMENT OF EOSINOPHILIC PNEUMONITIS

A CASE of pneumonitis with eosinophilia (Löffler's syndrome) successfully treated by intramuscular injections of emetine is recorded by T. Randall, of Durban (*British Journal of Tuberculosis and Diseases of the Chest*, January 1945, 39, 37). The patient was a coloured male, admitted to hospital with substernal pain of one month's duration, cough of two weeks' duration with copious purulent and blood-stained sputum, fatigue and anorexia. There were no night sweats or marked loss of weight

and no personal or family history of tuberculosis. The temperature varied between 99° F and 100 4° F and the pulse between 70 and 100, respirations were normal. There was increased vocal fremitus and vocal resonance in the upper third of the right lung and crepitations in the right apex and mid-zone. X-rays showed what was presumed to be characteristic tuberculous infiltration of both lungs, more marked on the right side. Blood sedimentation rate was 24 mm. in one hour. Sputum was negative for tubercle bacilli, amœbæ and fungi, and the stools negative for *Entamoeba histolytica*. Blood count showed Hb 14.2 gm. per cent., erythrocytes 4.3 million, colour index 1.1, leucocytes 9,600, with neutrophils 74 per cent., eosinophils 6 per cent., large mononuclears 1 per cent. and lymphocytes 19 per cent. The temperature settled to normal after six days' rest in hospital, otherwise the clinical picture was unchanged. Emetine was given daily by intramuscular route in injections of 1 grain for ten days. There was a dramatic and rapid response, the patient became symptom-free, the appetite improved, and X-rays taken twenty-five days after the first one showed clear lung fields. Apart from the presence of eosinophilia and the rapid improvement with emetine therapy there was no evidence of amœbic infection.

RECTAL PENICILLIN

IN a preliminary communication, L. Loewe, E. Altme-Werber, and P. Rosenblatt (*Journal of the American Medical Association*, May 5, 1945, 128, 18) provide data that suggest that the rectal administration of penicillin may prove satisfactory. Sodium penicillin, in amounts ranging from 300,000 to 1,000,000 Oxford units, was incorporated by hand in a cocoa butter base, and these suppositories were inserted without any preliminary preparation of the patient. Fourteen subjects were investigated (seven ambulatory, healthy volunteers and seven in-patients chosen at random). They were requested to retain the suppository as long as possible, and samples of blood were obtained hourly for twelve hours and then at the end of twenty-four hours. In no case was more than momentary discomfort caused by insertion of the suppository. In twelve cases appreciable blood titres, ranging from 0.012 to 0.768 Oxford unit per c.c.m. of serum were obtained, in two instances appreciable levels were found at the end of twenty-four hours, and in seven other instances effective titres were obtained four to twelve hours after insertion of the suppository. It is noted that the five most unsatisfactory results were obtained among the ambulant volunteers. The sustained minimum titre of 0.012 Oxford unit per c.c.m. is effective against a range of organisms including the gonococcus, pneumococcus and the hæmolytic

streptococcus Further work is being done in order to determine the optimum base and penicillin salt, as well as the best method of preparing the suppository

A DIRECTIONAL NEEDLE FOR SPINAL ANÆSTHESIA

IMPRESSED by the value of a directional needle for use in spinal anæsthesia, first described in 1931, S J Sarnoff and E A Rovenstine (*New York State Journal of Medicine*, February 1, 1945, 45, 286) have made an experimental and clinical investigation of its use. The feature of such a needle is that it has a bevelled point without an opening at its end, the fluid being delivered through a small aperture near the closed end. This opening is of such a size that it delivers fluid approximately one-half as rapidly as a needle with an open end



A niche on the hub of the needle indicates the direction in which the opening is facing. Among the advantages claimed for this type of needle are the following—(1) The extent of spinal anæsthesia can be controlled more easily and accurately, (2) the angle at which the needle is introduced has relatively little effect upon the extent of anæsthesia produced, as compared with the ordinary needle with which the extent of anæsthesia varies considerably with the angle at which the anæsthetic is introduced, (3) there is much less risk of aspirating cauda equina into the directional needle than into the standard model, (4) the risk of introducing some of the anæsthetic outside the spinal canal is reduced

GLUCOSE TOLERANCE

IN NEURO-CIRCULATORY ASTHENIA

IMPRESSED by the similarity of the symptoms in neuro-circulatory asthenia and those of hypoglycæmia, Major R A. Steven (*American Heart Journal*, March 1945, 29, 396) carried out glucose tolerance tests in forty soldiers with neuro-circulatory asthenia. In twenty-six of these (65 per cent) flat curves were obtained, the highest reading being less than 140 mgm. per cent. In most of the cases with a peak reading of 120 mgm. per cent or more, there was only one such reading and the rest of the curve was below 100 mgm. per cent. Of the remaining curves, eleven were normal, two were possibly diabetic and one was definitely diabetic. In view of the fact that there was no relationship

between the "faint spells," of which many of the patients complained, and eating, it is not considered that the low glucose levels are responsible for the symptoms of neuro-circulatory asthenia, this belief is supported by the finding that the ingestion of carbohydrate did not relieve these "attacks" as it would do were they due to hypoglycæmia. On the other hand, it is suggested that a low glucose tolerance curve may be of help in the diagnosis of neuro-circulatory asthenia

PENICILLIN CREAM IN THE TREATMENT OF SYCOSIS BARBÆ

THE results obtained in a series of twenty-one cases of sycosis barbæ by the use of a penicillin cream are recorded by A. Burrows, B Russell and H B May (*British Journal of Dermatology and Syphilis*, May-June 1945, 57, 97). The cream was prepared by autoclaving at 15 lb. for twenty minutes 250 ccm distilled water added to 50 gm. lanette wax SX, then 50 ccm. castor oil were sterilized by dry heat at 150° for one hour. After sterilizing, the two were mixed and cooled at 60°, and the appropriate amount of penicillin dissolved in water added to make the final concentration of 200 units per gm. This cream can be kept in screw-capped jars indefinitely, and when needed a jar can be warmed to 60° and penicillin solution added to obtain the required concentration. In all the treated cases bacteriological examination of the pus at the hair follicles or from beneath a crusted lesion was carried out, sensitivity tests were then put up from the primary cultures. When the predominant organism was found to be penicillin-sensitive, the patient was given a pot of cream containing 200 units of penicillin per gm. and instructed to apply it aseptically to the affected area. It is essential that strict asepsis be observed, the cream should be extracted from the jar or container with a sterilized knife-blade or spoon and spread on lint, the lid of the container being immediately replaced. The cream is applied two or three times a day and the patients return at intervals of not more than two weeks for fresh supplies or potency tests on the present supply. Of the twenty-one cases treated, in nineteen the condition was found to be due to a penicillin-sensitive strain of staphylococcus of thirteen with a history of more than one year, six were cleared within an average of six weeks, and six were improving over an average of this period. Four of the six patients with a history of less than one year were cleared in an average of two-and-a-half weeks, and one was improving over a period of five weeks. No improvement was obtained in two cases in which the condition was due to an insensitive strain of bacteria

REVIEWS OF BOOKS

Artificial Pneumothorax in Pulmonary Tuberculosis By T N RAFFERTY, M D
Introduction by HENRY STUART WILLIS, M D
London William Heinemann (Medical Books) Ltd, 1944. Pp xv and 192 Figures 26 Price 2/5

It is about fifteen years since artificial pneumothorax therapy came into common use, and published results have been numerous, with discordant opinions as to its value in the cure of pulmonary tuberculosis. With the advances in the technique of thoracoplasty during the past decade, the time is ripe for taking stock, and a critical review of pneumothorax treatment generally. Dr T N Rafferty has fulfilled this task well, and has formulated clear-cut indications and contraindications from first principles. Although he quotes extensively from other workers, there is a ring of practical and personal experience throughout the book. The chapters on tracheo-bronchial tuberculosis, the pathogenesis of cavity formation, and the complications of pneumothorax therapy are particularly good. He rightly stresses the importance of obtaining a selective collapse. The book is well produced, there is a good list of references, and the subject matter is clearly subdivided. It should prove valuable to those dealing with the treatment of pulmonary tuberculosis.

Psychology in General Practice Edited by ALAN MONCRIEFF, M D, F.R.C.P. "The Practitioner" Handbooks London *The Practitioner* and Eyre and Spottiswoode (Publishers) Ltd, 1945 Pp 199 Price 12s 6d

GENERAL practitioners who recognize how large a part the psychological side of illness plays in their work and how difficult it is to do it justice with no other equipment than that provided by common sense and the undergraduate medical curriculum, will find in this handbook much sensible and useful information. It is by no means a textbook of psychiatry, but has been designed to cover in a practical way those matters with which the practitioner constantly has to deal. His chief function in this direction, Professor Mullaix Culpin points out in an introductory chapter, should be "to recognize the nature of the troubles he meets, to let his patient feel that the troubles are understood, to teach him to give them their proper value, and to give him support and encouragement in carrying on with the job of living." Methods of examination and diagnosis, and the general principles of treatment are set out by Spencer Paterson,

R D Gillespie and Henry Wilson. In succeeding chapters the familiar types of neurosis are described by C H Rogerson, T M Ling, Helen Boyle and T J Hennelly, and a somewhat mussionary paper by James Halliday on "rheumatism" as a psychosomatic problem is followed by an exposition of the psychological problems of childhood and the minor degrees of mental defect by A. Alabert and D R MacCalman. The social side of psychiatry is emphasized in Desmond Curran's chapter on delinquency and in an account of psychiatric social work by Kathleen Edkins. A brief survey of the lines on which problems of sexual adjustment can be handled, by E F Griffith, and an informative and admirably concise description of the procedure for mental hospital admission and discharge by S R. Tattersall, conclude a manual which is temperate, lucid and well suited to its purpose.

NEW EDITIONS

ALTHOUGH less than two years have elapsed since the publication of the third edition of *Diseases of the Nervous System*, by F M R WALSHE, O.B.E., M.D., D.Sc., F.R.C.P., the many advances in the diagnosis and treatment of nervous disorders that have taken place in that time have called for a new edition. The fourth edition (E & S Livingstone Ltd., 1951) contains among the new additions a section on the use of synthetic vitamin B₁ in the treatment of multiple peripheral neuritis, new material in the section on cervical rib pressure in the chapter on muscular atrophies, and mention of the somewhat rare condition known as larvageal epilepsy. Some new illustrations have been added.

Textbook of Medicine, edited by J J CONYBEARE, M.C., D.M., F.R.C.P., in its seventh edition (E & S Livingstone Ltd, 30s) contains a new section on the sulphonamides and another on sarcoidosis. Considerable rewriting has been undertaken, particularly in the chapters dealing with diseases of the respiratory system, renal diseases, and diseases of the cardiovascular system.

The Infant A Handbook of Management, by WILFRED J PEARSON, D.S.O., M.C., D.M., F.R.C.P., and ARTHUR G WATKINS, B.Sc., M.D., F.R.C.P., in its third edition (H K Lewis & Co Ltd, 4s) contains two new sections dealing respectively with preventive inoculation and vitamin requirements, values and sources. In the inoculation section the site of injection, material advised and dosage for different ages are given, and the vitamin section contains a list of preparations with approximate vitamin content and daily dosage.

NOTES AND PREPARATIONS

MEDICAL AUXILIARY SERVICES

THE National Register of Speech Therapists, 3rd edition, 1944, and of Chiropodists, 5th edition, 1944-45, have just been issued. The former gives, in addition to the private or professional addresses of qualified speech therapists, a list of hospitals and local authorities which employ registered medical auxiliary speech therapists. The address, for purposes of registration, of this qualifying body is the College of Speech Therapists, 86 Harley Street, London, W 1. An example of the growing importance of this branch of auxiliary medical work is shown by its inclusion in the draft Regulations published by the Ministry of Education, providing for special training by a qualified speech therapist for any child suffering from speech defect. In connexion with the register of chiropodists, it is of interest to note that a memorandum on the relationship of chiropody and the health of the community has been prepared by the Council, copies of which can be obtained from the Chiropody Group Council, B.M.A. House, Tavistock Square, London, W C 1. Practitioners requiring copies of either, or both, registers should apply to the Acting Secretary, Board of Registration of Medical Auxiliaries, B.M.A. House, Tavistock Square, London, W C 1. They are supplied free of charge.

OFFICIAL NOTICES

Cancer Act, 1939 (Circular 91/45) refers to the new issue of cards for the recording of treatment and follow-up of cancer patients, and of a pamphlet giving instructions for the use of the cards, both of which are being issued to Main Treatment Centres by the Radium Commission. *Nutritive Values of Wartime Food* (Medical Research Council War Memorandum No. 14), which is obtainable from H.M. Stationery Office, price 1s, contains tables compiled for the Accessory Food Factors Committee, giving the nutritive value of cereals, meats, fish, fruits, fresh, canned and dried, vegetables, fresh and canned, sweets and preserves, beers, nuts and offals. The protein, fat, carbohydrate, calorie, calcium, iron and vitamin contents of the different articles are given, and in the case of meats and fish the nutritive value of the different parts of the animal or fish purchased. Food concentrates are also included, and tables giving the most important sources of vitamin D and riboflavin.

AMERICAN LIBRARY U.S. OFFICE OF WAR INFORMATION

RECENT publications issued by the American

Library of the U.S. Office of War Information include a symposium on "Amputations" and another on "Tropical Diseases," both of which are reprinted from the *Journal of the American Medical Association*, of April 8 and 26, 1944, respectively. Another reprint of interest deals with the subject of "Arthropod-Borne Diseases," and their prevention and control. The work, which is a reprint from *War Medicine*, May/June, 1943, deals with the subjects of malaria, dengue, yellow fever and a number of other diseases carried by arthropods. The address of the Library is the American Embassy, 1, Grosvenor Square, London, W 1.

LEAFLET FOR PATIENTS WITH ANGINAL PAIN

A LEAFLET entitled "Advice in Cases in which Exertion Causes Pain in the Chest," suitable for distribution to patients, and reprinted from the article by J. W. Linnell and W. A. R. Thomson in *The Practitioner*, 1939, 142, 377, is again available. It may be obtained from The Practitioner Office, 5, Bentinck Street, London, W 1, price 1s per dozen.

SCOTT'S EMULSION

IN Dr Cecile Asher's article on "Vitamin Dosage" (*The Practitioner*, March 1945, 154-163) the vitamin content of Scott's Emulsion was wrongly given, having been calculated on the basis of a minimum standard B.P. cod-liver oil. The vitamin potency of this emulsion is in fact much higher and, as stated on the label, amounts to 10,000 I.U. of vitamin A and 2,400 I.U. of vitamin D per fluid ounce. Practitioners who have secured reprints are asked to make the necessary alteration in table 7.

CONTENTS FOR SEPTEMBER, 1945

NUTRITION

Standards of Food Requirements By Professor

J. R. Marrack, D.S.O., M.C., M.D.

Nutrition from the Standpoint of Public Health.

By E. H. Marcus Milligen, M.D., D.P.H.

Diet and the School Child By R. E. Smith,

M.B., F.R.C.P.

Cooking and Nutritional Value of Food By

G. Neil Jenkins

Hospital Diet By Miss R. Pybus, O.B.E., S.R.N.

Child Health XV—*Care of the Blind Child*

By R. R. Garden, M.B., D.P.H., D.O.M.S.

THE PRACTITIONER

No 927

SEPTEMBER, 1945

Volume 155

STANDARDS OF FOOD REQUIREMENTS

BY PROFESSOR J. R. MARRACK, D.S.O., M.C., M.D.

*Professor of Chemical Pathology, University of London, Chemical Pathologist,
London Hospital*

THE attempt to establish dietary standards involves a decision on the purpose that the standards are intended to serve. The Hot Springs Conference adopted the standard of the National Research Council of the U.S.A. as a "tentative goal towards which to aim" which would ensure for human beings a high level of health and vitality, so far as this can be effected by diet. It was recognized, however, that "lower levels of intake of minerals and vitamins are compatible with a good general state of nutrition, although doubtless health could be improved if the full allowances were obtainable." The special joint Committee of the Combined Food Board that drew up the report on *Food Consumption Levels* (1944) adopted the "70 per cent. minimum standards"—the N.R.C. figure for calories and protein in all cases and for minerals and vitamins in respect of the groups up to the age of twenty and pregnant and nursing women, and 70 per cent. of the N.R.C. allowances for minerals and vitamins for adult men and women (other than pregnant and nursing). Bacharach and Drummond (1940) attempted to be more precise and proposed two standards—an optimal, corresponding to the N.R.C. standard, and a minimal, defined as one "that if consumed for a considerable time—say six months or a year—would not result in the appearance of any untoward change that would not be reversed by substitution of a diet nearer the optimal."

The acceptance of such sub-optimal standards involves the assumption that intermediate states between optimal nutrition and gross deficiency may occur in human beings. The occurrence of such intermediate states can be clearly demonstrated in experiments on animals. It could hardly be disputed that there are degrees of health and development in children, corresponding to different levels of nutrition. Also, apart from gross deficiency diseases, health and efficiency of adults vary with their diet, but other factors which affect health almost invariably vary along with diet. In McGonigle's (1933) study, which suggested that food was more important than housing, the numbers studied were small. But it may be said that during this war an enormous experiment—McGonigle in reverse—has been carried out. The nutritive value of the diet has been maintained or improved, whilst other factors have deteriorated. This maintenance and improvement of health are strong evidence that improvement in food can do more than prevent gross deficiency diseases. In the earlier years many reports appeared in which it was claimed that the consumption of extra vitamins raised the level of health, in particular, that additional vitamin A would lower the frequency or severity of colds. But, during recent years, carefully controlled experiments have been carried out which give no evidence of any such improvement, and in several

experiments it has been found that human beings can live for several months without any deterioration of health and efficiency, although taking far smaller amounts of one or the other nutrient than has been considered necessary. There has, in consequence, been a swing away from the acceptance of any particular standard of food requirements.

In the case of the vitamins of the B group the position has become complicated by the demonstration that aneurin, riboflavin and nicotinic acid can be synthesized by bacteria in the human intestine. There is evidence that aneurin and nicotine, so formed, can be absorbed and can supplement, or even take the place of, the supply of these vitamins in food. In view of these developments it becomes necessary to reconsider standards of requirements, particularly minimum standards.

ASCORBIC ACID

The best examples of intermediate states of deficiency in adult animals is seen in guinea-pigs supplied with less than optimum amounts of ascorbic acid. An allowance of 0.5 mgm per day is enough to prevent scurvy, and to prevent loss of weight, but if no more is allowed, healing of wounds and repair of fractures fail. As the allowance of ascorbic acid is increased, healing and repair steadily improve. But the tension needed to break down a wound does not increase further nor the rate of repair of fractures improve when the daily allowance is raised to about 5 mgm per day. The optimum requirements of guinea-pigs can therefore be fixed precisely at 5 mgm per day.

Experimental signs of deficiency—Gothlin's (1937) estimate of human requirements was based on experiments in which capillary fragility was increased and the gums became swollen and bled after about two months on diets containing minimal amounts of ascorbic acid. The amount of ascorbic acid in the diet was then increased and the level at which the capillary fragility returned to normal was taken as the minimum requirement. However, it is now generally held that increase of capillary fragility is not due to ascorbic acid deficiency; in Crandon's (1940) experiment the fragility was not increased after nine months on a diet which contained practically no ascorbic acid. Whilst gingivitis is not necessarily an early sign of ascorbic acid deficiency, undoubtedly it is one of the outstanding features of scurvy, and the gingivitis of scurvy clears up spectacularly when ascorbic acid is given. But it seems that some other factor besides lack of ascorbic acid may be involved. Crandon's gums were not swollen and did not bleed after nine months on the deficient diet. Towards the end of these nine months an experimental wound made in Crandon's back was not healed ten days after it was made. A wound made after three months on the deficient diet appeared, on microscopic examination, to heal normally. It might be objected that there is considerable variation in this "normal" rate of healing of wounds, it is quite possible that the wound would have healed still more rapidly if Crandon had not been depleted of ascorbic acid.

The earliest evidence of deficiency in this experiment was fatigue, which was noticeable after sixty days. Rietschel and Mensching (1939) in a similar experiment claimed that there was no decline in muscular efficiency in 100 days. Johnson *et al* (1945) report an experiment on volunteers in a civilian public service camp

the group was given a diet in which ascorbic acid had been destroyed, a second a similar diet supplemented with 75 mgm. of ascorbic acid per day; a third an ordinary camp diet, containing 56 to 109 mgm. of ascorbic acid per day, and fourth the camp diet supplemented with 75 mgm. of ascorbic acid per day. As a test of physical efficiency all four groups improved during the experimental period of eight weeks. In one only of the first group, and in none of the other groups, the gums became slightly spongy and bled easily at the end of the deficiency period, the gums became normal within ten days when the daily intake of ascorbic acid was raised to 500 mgm. Otherwise there was no evidence that the deprivation of ascorbic acid caused an objective or subjective deterioration.

More should not be inferred from these experiments than the conditions of the experiments justify. Even under adverse conditions four to eight months elapse before scurvy appears. It cannot be inferred that, because there is no evidence of deterioration in two months, under favourable conditions, low intakes prolonged over many months, under adverse conditions, may not have serious effects. Undoubtedly gingivitis is not a specific sign of ascorbic acid deficiency, most cases are due to some other cause, and other factors probably cooperate with lack of ascorbic acid in its causation. But the gingivitis of actual scurvy is indisputable, and in some instances it appears that gingivitis may be caused by lack of ascorbic acid and be curable by ascorbic acid without other evidences of scurvy. There is evidence that healing after operations may be delayed when the concentration in the plasma is low and improved by the administration of ascorbic acid. Campbell and Cook (1942) claim that healing after extraction of teeth is more rapid and bleeding less if a large dose of ascorbic acid is given before extraction. It has been claimed that hæmorrhage after cataract extraction is reduced by administration of ascorbic acid (Urbanek and Albrecht, 1938, Malling, 1938). However, assessment of the relation of healing after operations on human beings would need a very long series of cases, with controls. Pirie (1945) found that saturation with ascorbic acid, before operation, did not reduce the incidence of hyphæmia after cataract extraction. 'It is possible that a high concentration of ascorbic acid in the body fluids may help in dealing with special emergencies. The doses of ascorbic acid used by Campbell and Cook would raise the concentration for a short period only and have a negligible effect during the greater part of the healing period.'

Human requirements—No estimate of requirements can be based directly on estimates of the amount needed to saturate with ascorbic acid or to maintain a certain level in plasma or leucocytes. It is first necessary to decide whether saturation or any particular level in the blood is necessary for maintenance of health and efficiency. There is little evidence for saturation as a standard. At saturation point the concentration of ascorbic acid in the plasma is in the neighbourhood of 0.8 mgm. per 100 c.c.m. But animals that make their own ascorbic acid normally maintain concentrations of from 0.3 to 0.56 mgm. per 100 c.c.m. of ascorbic acid in their plasma. The concentration in the plasma of guinea-pigs, receiving the optimum dose of 5 mgm. per day, is about 0.4 mgm. If inferences can be drawn from these observations on other animals the physiological range is between 0.3 and 0.6 mgm. per 100 c.c.m., these levels would be maintained in an adult by a daily intake of from 30 to 60 mgm. per day.

In an experiment reported by Pijoan and Lozner (1944) one of the authors lived for twenty-two months on 25 mgm or less of ascorbic acid daily, again without any sign of deterioration. The ascorbic acid in the plasma ranged between 0.0 and 0.2 mgm per 100 c cm, but remained at 26 mgm in the leucocyte-platelet layer for eighty days when the daily intake was 18 to 25 mgm. An experimental wound healed normally and no ill-effects were observed. It is probable that the concentration in leucocytes is a better indicator of adequacy of the ascorbic acid supply than the level in the plasma.

These studies of ascorbic acid requirements illustrate the difficulties involved in establishing standards. The requirements of other animals may not even be qualitatively the same as those of human beings and not quantitatively equal, even when the same qualitatively. Guinea-pigs require much more of ascorbic acid per kgm of body weight than do human beings to maintain the concentration in the blood at a given level or to prevent the appearance of signs of deficiency. The estimate of requirements may be based on the amount needed to prevent or cure the earliest signs of deficiency. But these earliest evidences of deficiency are not specific and may vary with conditions. The effects of prolonged sub-optimal intake (corresponding to the intermediate state in guinea-pigs) may differ from those of relatively short and extreme deficiency. It is difficult to define and recognize intermediate states in man. It is essential that any experiments in which the effects of varying amounts of ascorbic acid on a group of subjects are studied should be controlled by observations on a group of subjects living under conditions which are identical except in respect of ascorbic acid. No conclusions as to the amounts needed to maintain health over long periods can be drawn from experiments lasting a few months only. The best evidence on human requirements that has been obtained is given by the experiments of Najar and his colleagues (1944), in which seven young adults lived for eighteen months on a constant daily intake of 25 mgm of ascorbic acid without developing any detectable abnormality, and by the observations of Stamm, Macrae and Yudkin (1944) that no disability attributable to deficiency of ascorbic acid appeared among nearly 3,000 R.A.F. personnel on diets that supplied from 17 to 26 mgm of ascorbic acid daily.

ANEURIN

Recent experiments on requirements of aneurin have run along three lines —

- (1) Several investigators have found some evidence of deficiency, after periods of a month or more, in subjects eating diets that supplied not more than 0.22 mgm of aneurin per 1000 calories. This group includes experiments made by Williams and her colleagues (1942) with diets that contained varying amounts of aneurin supplemented with other members of the B group. In particular they found that when the intake was limited to 0.22 mgm of aneurin per 1000 calories, symptoms appeared in from one to three months and that these symptoms did not completely disappear unless the intake of aneurin was 0.5 mgm per 1000 calories.
- (2) Najar and Holt (1943) found that four out of nine young men who had lived for many months on diets supplying 0.1 mgm per day continued on diets containing no aneurin for seven weeks. They found that the faeces

of these four contained 10 to 25 times as much vitamin B₁ as the faeces of those who showed signs of deficiency. They concluded that aneurin was made by bacteria in the intestines of these resistant subjects and that enough was absorbed to protect them against deficiency.

- (3) Nevertheless, all the subjects of Najjar and Holt maintained weight and vigour when taking only 0.1 mgm. of aneurin per day. Ancel Keys and his colleagues (1943) also found that young men could maintain health and full capacity for exhausting work for ten to twelve weeks on an intake of only 0.23 mgm. of aneurin per 1000 calories. The amount of aneurin excreted in the urine of these subjects did not suggest that they were obtaining appreciable amounts of aneurin from bacterial synthesis.

Signs of deficiency—It may be objected that the evidence of deficiency in the experiment of Williams and colleagues quoted above were subjective and might be due to the monotony of the diet or other experimental conditions. However, these symptoms cleared up when doses of aneurin were given without the subject's knowledge and without any other changes in the diet. Also objective evidences of deficiency appeared in about three months in another experiment (Williams *et al*, 1943) in which the average daily intake of aneurin was 0.175 mgm. per 1000 calories. Another objection is that the subjects of these experiments were women who had recovered from "psychiatric abnormalities." It might be supposed that their nervous systems might be particularly vulnerable, or that they might have some underlying metabolic disturbance which demanded large daily supplies of neurin. This objection is answered by experiments on normal subjects, such as those of Egaña *et al* (1942), Barborka *et al* (1943) and Archdeacon and Murlin (1944) in which subjective and objective evidence of deficiency were found in periods of from four to nine weeks on diets supplying up to 0.64 mgm. of aneurin per day. It appears that the absorption of adequate amounts of aneurin, formed by bacteria in the intestine, is exceptional.

Daily requirements—Ancel Keys and his colleagues (1943, 1944) point out that no conclusion can be drawn as to aneurin requirements for longer periods. Although it may be possible to continue for months on the lower levels under favourable conditions without any loss of health and efficiency, it would be advisable to retain the Board of Nutrition Standards of 1.8 and 1.5 mgm. per day for moderately active men and women (0.6 mgm. per 1000 calories) until there is further proof that these large amounts are unnecessary.

NIACIN

The announcement by Ellinger and his colleagues (1944, 1945) that nicotinic acid is synthesized by bacteria in the intestine and that the amount so synthesized may be as much as 80 per cent. of the estimated human requirements, offers a solution of the puzzle of the incidence of pellagra. For pellagra does not necessarily appear among populations whose intake of niacin is low and, although commonly associated with maize, may occur when no maize is eaten. Milk, which is regarded as a fair foodstuff for preventing or curing pellagra, contains relatively little niacin, presumably milk in the diet favours the formation of nicotinic acid by bacteria in the intestine. It appears that the actual amount of nicotinic acid in the diet is

no measure of the efficiency of the diet in supplying the body with niacin, although a high content rules out deficiency, a low content does not necessarily mean that the amount absorbed will be too low

RIBOFLAVIN

There is, as yet, no evidence that riboflavin formed by bacteria in the intestine is used by human beings to supplement that contained in the food. Sebrell *et al.* (1941) found an intake of about 0.2 mgm per 1000 calories (or 0.5 mgm per day) insufficient to prevent cheilosis, the cheilosis was cured when the amount was raised to 0.025 mgm per kgm. of body weight (about 1.3 mgm per day) or in one case 0.05 mgm per kgm. Ancel Keys *et al.* (1944) found no sign of impairment of health and efficiency in six normal young men, who lived on a diet that supplied, on an average 0.99 mgm per day (or 0.31 mgm per 1000 cal) for from 84 to 152 days. An outbreak of stomatitis occurred in a camp in Africa after a change in the diet which reduced the average intake of riboflavin from 1.6 to 1.0 mgm per day (about 0.35 mgm per 1000 cal). Cases of stomatitis still occurred when the diet was changed to one supplying 1.28 mgm per day; the outbreak ceased when the diet supplied 1.7 mgm per day (Jones *et al.*, 1944). Macrae, Barton Wright and Copping (1944) estimated the riboflavin in the actual food provided in messes of the R A F. The average amount per day ranged from 1.5 to 2.6 mgm., with a mean value of 1.9 mgm. No signs of deficiency were found among a large number of R A F personnel examined by Lyle, Macrae and Gardiner (1944). It may be assumed that an intake over 1.5 mgm per day is satisfactory.

VITAMIN A

The first sign of deficiency on which estimates of requirement of vitamin A are based is impairment of dark adaptation. However, recent studies indicate that evidence of impairment of dark adaptation does not appear until after a longer period of deficient intake than had formerly been supposed, the deductions drawn from experiments in which it appeared that adaptation was impaired after relatively short periods may be invalid. After long periods of deficiency, stores of vitamin A in the liver are depleted, the doses of vitamin A then needed to restore dark adaptation may be used largely to refill this depleted store and may be no measure of the amount required for maintenance. Thus requirements of vitamin A may be less than supposed. On the other hand, absorption of carotene by human beings appears to be variable, when carotene is the main source of vitamin A, the requirements may be more generous than the usual estimates.

GENERAL CONCLUSIONS

Experiments in which it is found that adults can maintain health for limited periods, under favourable conditions, on low intakes of certain nutrients, have no bearing on the requirements during childhood, pregnancy and lactation. Nor should they lead to under-estimation of the requirements of sick persons. Elsom and collaborators (1942) found that one of their subjects, living on a marginal intake of aneurin (0.28 mgm per 100 calories) developed symptoms of deficiency after an attack of tonsillitis.

When the relatively non-soluble sulphonamides, such as succinyl sulphathiazole, that inhibit bacterial growth in the intestine, are used, generous amounts of the

group of vitamins should be given to make up for loss of synthesis by the bacterial

Also, when other sulphonamides are administered it is advisable to increase allowances of these vitamins, as the sulphonamides may interfere with their action (Ellinger and Benesch, 1945)

Experiments such as those reported by Bransby *et al* (1944) show that supplements of individual nutrients or mixtures of nutrients do not have the beneficial effect of good food

It now appears that the nature of the food can affect the supply of a vitamin through its influence on synthesis by bacteria in the intestine There is a growing body of evidence of the interaction between various nutrients, as between vitamin A and tocopherol These newer developments cast doubt on the validity of marginal standards of diet based on estimates of minimal requirements of nutrients considered separately

The interrelation of vitamins is further illustrated by the experiments of Richards (1943, 1945) In the first, the addition of aneurin alone to a poor diet seemed to have a harmful effect on the growth of suckling rats and the condition of their mothers In the second, large amounts of aneurin and chalk added to a pyridoxin-deficient diet provoked symptoms of pyridoxin deficiency These experiments show the unsoundness of supplementing white flour with vitamin B₁ and calcium, without other nutrients, such as pyridoxin, and the fallaciousness of assessments of the nutritive value of flours based on estimations of aneurin only

References

- Archdeacon, J W, and Murlin, J R (1944) *J Nutr*, **28**, 241
 Bacharach, A L, and Drummond, J (1940) *Chem Ind*, **59**, 37
 Barborka, C J, Foltz, E E, and Ivy, A C (1943) *J Amer med Ass*, **122**, 717
 Bransby, E R, *et al* (1944) *Brit med J*, **1**, 77
 Campbell, H G, and Cook, R P (1942) *Brit dent J*, **72**, 6
 Crandon, J H, Lund, C C, and Dill, D B (1940) *New Eng J Med*, **223**, 353
 Egaña, E R, *et al* (1942) *Amer J Physiol*, **137**, 731
 Ellinger, P, *et al* (1944) *Nature*, **154**, 270
 —, and Benesch, R. (1945) *Lancet*, **1**, 432
 Elsom, K. O, *et al* (1942) *Amer J med Sci*, **203**, 569
 Food Consumption Levels in the United States, Canada and the United Kingdom (1944) H M Stationery Office
 Göthlin, G F, *et al* (1937) *Act Med Scand*, **92**, 1
 Johnson, R E, *et al* (1945) *J Nutr*, **29**, 155
 Jones, H E, *et al* (1944) *Lancet*, **1**, 720
 Keys, A., *et al* (1943) *J Nutr*, **26**, 399
 — (1944) *Ibid*, **27**, 165
 Lyle, T K., Macrae, T F, and Gardiner, P A (1944) *Lancet*, **1**, 393
 Macrae, T F, Barton-Wright, T F, and Copping, A. M (1944) *Biochem J*, **38**, 132
 M'Gonigle, G C M (1933) *Proc roy Soc Med*, **27**, 677
 Malling, B (1938) *Med Rev*, **55**, 280
 Najar, V A., and Holt, L E (1943) *J Amer med Ass*, **123**, 683
 —, and Royston, H M (1944) *Johns Hopk Hosp Bull*, **75**, 315
 Pijoan, M., and Lozner, E L (1944) *Ibid*, **75**, 303
 Pirie, A. (1945) *Brit J Ophthal* (in press)
 Richards, M B (1943) *Brit med J*, **2**, 418
 — (1945) *Ibid*, **1**, 433
 Rietschel, H., and Mensching, J (1939) *Klin Wschr*, **18**, 273
 Sebrell, W H, Jun, *et al* (1941) *Pub Hlth Rep Washington*, **56**, 510
 Stamm, N P, Macrae, T F, and Yudkin, S (1944) *Brit med J*, **2**, 239
 Urbaneck, J., and Albrecht, W (1938) *Ztschr Augenheilk*, **95**, 129
 Williams, R D, *et al* (1942) *Arch int Med*, **69**, 712
 — (1943) *Ibid*, **71**, 38

NUTRITION FROM THE STANDPOINT OF PUBLIC HEALTH

By E H M MILLIGAN, M D, D P H

Medical Officer of Health, Glossop

WHILST the maintenance of body nutrition is directly the responsibility of the individual in the case of adults, and of parents, foster parents and other guardians in the case of children, the community as a whole has also considerable responsibility, so in this respect what can be done by organized communities will be included in what is here written

Before starting to write about nutrition it is necessary to have a clear idea of what is meant by the term. The word "nutrition" is not a good one as it puts the stress too much on food, whereas what is now involved, in what is generally understood by the term, is the physio-chemistry of life. For instance, McCarrison (1937) defines it as "the sum of processes concerned in the growth, maintenance and repair of the living body as a whole and its constituent parts," and goes on to describe the factors concerned with good nutrition—

- (1) Adequacy of materials—food, water, oxygen, sunlight.
- (2) Efficient use of materials
- (3) Exercises of the body as a whole, its organs and parts, also its adaptive functions, i.e., to variations of food, temperature, rain, wind, sun, clothing, altitude, work, sexual activity
- (4) Rest and sleep
- (5) Avoidance of adverse influences, i.e., emotional or other worry, infection, bad ventilation, fumes and dust and dietetic vices, such as over-indulgence in sugar, tobacco or alcohol

The term as used now means even more than this, for it is applied not only to processes but to the condition of the body resulting from those processes, so that the terms good or bad nutrition, or "under-normal" nutrition, are commonly used and are applied to the body in the static condition resulting from past nutritive activities (i.e., the body has an adequate or inadequate amount of food on it or shows some deformity or lack of repair) and, going further, the nutritional state of the body is judged according to functional activities, as strength, endurance or respiratory or circulatory effort, and such-like

To get one term to give an inclusive meaning to all this would be perhaps impossible, although some words like "physical and nutritional condition," or to get the meaning in one word, "kinetrophy" *—expressing activity associated with nourishment or "nutreffiency" might do

Nutrition then, for the purpose of this article, covers what has been mentioned above, and the problem that will be considered is how the community (i.e., central or local authority) and organized medicine, in its widest sense, can promote this

* Biotrophy is another suggestion—nourishment in association with the maintenance of life

'nutreffiency' or good "kinetrophic" condition in the population of all ages and sexes

Now to promote this nutreffiency of the population. first, there must be methods of testing so as to ascertain whether or not individuals or groups reach certain standards of efficiency; secondly, the cause or causes of any deficiency found must be determined, and, thirdly, the measures necessary, not only to prevent deficiency but to establish positive and full efficiency, must be instituted

ASSESSMENT OF THE PHYSICAL AND NUTRITIONAL CONDITION
This side of the question has been mentioned by Professor Marrack in the opening article of this issue but it may be permissible to say that there is no pathognomonic test for the nutritional state, it can only be assessed in different categories as follows —

- (1) A general clinical evaluation
- (2) Weight for age.
- (3) Skeletal size (not height only) for age
- (4) Weight for skeletal size
- (5) Muscularity
- (6) Growth rate in weight and skeletal size
- (7) Strength for age per lb. or kgm. of body weight
- (8) Endurance per total energy (fatigue resistance potential and per lb. or kgm. of body weight)

The general practitioner should make himself acquainted with the tests in addition to taking heights and weights at stated periods (say, quarterly), and should learn to use a dynamometer to test body strength, he should learn to estimate endurance by getting the individual to be tested to hang on to a horizontal bar with feet clear of the ground, the time being recorded in seconds

Although comprehensive standards are not available, some data relating to these tests have already been published (Milligan, 1945)

If the practitioner, by clinical examination or use of some of the tests mentioned, comes to the conclusion that nutri-deficiency is suspected or seems definite, he should report the case to the local medical officer of health so that more thorough investigations (including environmental conditions) can be made

Investigation of the causes of nutri-deficiency — This will include investigation of the factors mentioned by McCarrison as affecting nutrition, such as (a) adequacy of food, water, oxygen, and sunlight, (b) proper use and assimilation of the foregoing; (c) body exercise and body adaptations to such things as temperature, clothing, altitude, (d) adequacy of rest and sleep, (e) adverse influences involved, such as worry, infection, and bad ventilation

It is impossible, in a short article, to go into all these matters in detail, but it may be profitable to consider some points in connexion with a few of them and, as food is one of the prime matters involved, the question of adequate dietary will be considered.

DIET IN RELATION TO NUTRITION

In dealing with dietaries it is not sufficient to investigate just one or two probable deficiencies in any particular dietary but it is essential to see that the diet as a whole

TABLE 1
DAILY DIETARY REQUIREMENTS (adapted from Bacharach and Drummond, 1940)

Protein (gm)	Fat (gm)		Calories (heat units)	Calcium gm	Phos- phorus gm	Iron gm	A I U	B ₁ mgm	C mgm	D* I U	Lactoflavin or Riboflavin mgm	Niacin mgm	Adernin mgm
	Plant	Animal											
Animal													
Marginal 30	20	30	20	0.75	1.0	0.010	2500	1	25	400	1	5	50
Optimum 50	50	100	20	1.5	1.5	0.020	7500	3	75	500			

Note—Optimum protein retention varies from 4 gm per kgm (2 046 lb) for children 1 to 3 years, to 2.5 gm for those from 13 to 15 years

*Two-third calories should be from milk, dairy products, fruit and vegetables, including potatoes (Boyd Orr 1939)

Corry Mann (1939) states that public schoolboys' diet contained from 54 to 62 per cent of animal protein as compared with 35 to 36 per cent in the industrial group of children

* More for expectant and nursing mothers and young children, e.g., the mothers 800, young children 1000 Also vary for age adults over forty years, 300

is not only a minimum one to prevent detectable nutri-deficiency or malnutrition, but adequate to promote positive or robust health, including in adults the maintenance of reproduction to be carried on from one generation to another

In table 1, standards of marginal and positive health dietaries are given. It will be seen that figures are given under certain headings, such as protein, calories (the head-producing power of the diet), fat, minerals and vitamins, and not in the details of actual food, so that it will be necessary to consult reliable reference books to calculate the constituents of the foods to be eaten in food values.

The book I advise for this purpose is "Modern Dietary Treatment" by Abrahams and Widdowson (1940) †. This book, in addition to giving food values, gives the details of diets suitable for different diseases and also a considerable amount of general information regarding nutrition.

To give an example of the food values of a dinner—Supposing someone gets 2 oz grilled beefsteak, 4 oz potatoes (boiled), 3 oz cabbage and 4 oz semolina pudding; from this book it would work out as follows—

Beef protein 14.2 gm., fat 12.2 gm., calories 172, calcium 5.2 mgm., phosphorus 172 mgm., iron 2.96 mgm.

Potatoes protein 1.6 gm., calories 100, calcium 4.8 mgm., phosphorus 32.8 mgm., iron 0.56 mgm., vitamin A 48 I U, vitamin B₁ 36 I U, vitamin C 12 mgm. (average)

Cabbage protein 6 gm., calories 6, calcium 37.5 mgm., phosphorus 20.4 mgm., iron 0.4 mgm., vitamin A 800 I U, vitamin B₁ 4.8 I U, lactoflavin (riboflavin) 0.042 mgm., vitamin C 51 mgm.

Semolina pudding protein 4.8 gm., fat 4.4 gm., calories 152, calcium 136 mgm., phosphorus 120 mgm., iron 0.16 mgm.

The meal as a whole would then be found to contain—

Protein 26.6 gm., fat 16.6 gm., calories 430, calcium 183 mgm., phosphorus 345 mgm., vitamin A 848 I U, vitamin B₁ 40.8 I U, vitamin C 63 mgm., vitamin D, lactoflavin (riboflavin) 0.042 mgm.

Compare these totals with the amounts necessary per table 1, and the first thing that will be noticed is the lack of balance in the constituents, for instance, vitamin C is in good quantity, and vitamin A and vitamin B₁ and riboflavin are woefully short. Other constituents are, of course, short also, but not in so unbalanced a way. An additional type of meal is therefore necessary, one rich in vitamin B₁ and riboflavin and which will also make good the shortages in the other constituents, e.g., protein, fat, calories and minerals.

Wholemeal bread, butter, cheese, milk and some other foods, such as fat, fish or meat or eggs, are needed (refer to the food values of these). If the deficiencies were not made good, what would happen? Take protein and suppose that school-boys* of the industrial or elementary school type have to be dealt with. It has been mentioned that this type of child's animal protein is about 36 per cent of total protein as compared with 54 to 62 per cent of the public schoolboys. In Glossop, in 1937, a dietary survey gave the values of protein per unit of population (0.8 man value equalling the value of a boy of about eleven years) as 21.8 gm animal and 32.7 gm vegetable protein. The total amount of protein being 64.5 gm. per 0.8 man value or 80 gm whole man value. For a full-grown man, 80 gm would be above the marginal need, but for a growing boy, who not only

† Also—"Manual of Food," 1945, H M Stationery Office

* See table 1, footnote

needs to replace wastage but to form additional flesh, the amount is insufficient, especially in animal protein, as the percentage is about 36·7 of the total protein. Now actually in weight and height growth the Glossop elementary schoolboys' weights and heights showed much less growth (as outlined in table 2) than public schoolboys at Christ's Hospital (see table 2)

TABLE 2
HEIGHTS AND WEIGHTS OF ELEMENTARY SCHOOLBOYS, GLOSSOP (1936-40), AND CHRIST'S HOSPITAL (PUBLIC SCHOOL) BOYS

	No tested	Mean age		Mean weight in lb	Mean height in inches
		Years	Months		
Nine years					
†Free meals children	20	9	0	56 88	49 8
Employed's children	34	9	1	61 5	51 5
*Christ's Hospital, 1930-33				68 06	52 72
Ten years					
†Free meals children	25	10	1	63 7	52 7
Employed's children	32	10	1	64 8	53 4
*Christ's Hospital, 1930-33				73 35	54 33
Eleven years					
†Free meals children	39	11	1	62 4	52 6
Employed's children	138	11	1	69	55 6
*Christ's Hospital, 1930-33				78 63	56 70
Twelve years					
†Free meals children	78	12	1	72 3	54
Employed's children	191	12	1	77 8	56 8
*Christ's Hospital, 1930-33				85 92	57 74
Thirteen years					
†Free meals children	68	13	1	79 5	57 6
Employed's children	159	13	0	81 8	57 2
*Christ's Hospital, 1930-33				94 36	60 0
Fourteen years					
†Free meals children	42	13	10	85 6	58 5
Employed's children	117	13	10	92	59 7
*Christ's Hospital, 1930-33				106 56	62 50

† Children of the unemployed * G E Friend, "The Schoolboy," (1935)

At nine years of age, Christ's Hospital public schoolboys were, on the average, about 11 lb heavier and 3 inches taller than ten-year-old "unemployed's" Glossop elementary schoolboys, at ten years, about 9 5 lb and 1 63 inches more, at eleven years, 16 lb and 4 inches more, at twelve years, 13 75 lb and 3 75 inches more, at thirteen years, 14 8 lb and 2 4 inches more, and at fourteen years, about 21 lb and 4 inches more. Elementary schoolboys of employed parents in Glossop were not quite so stunted (as compared with the public schoolboys as their school mates whose parents were unemployed, but still they, too, were much below the average public school weights and heights).

In Glossop also, in 1941, when protein in England was in short supply,* boys of eleven years were found to be growing in weight and height only 48 per cent. and 79 per cent of the pre-war rate. Protein is, of course, essential for body growth and maintenance, especially animal protein, as it contains the amino-acids necessary for growth, such as tryptophane, histidine, cystine and lysine. Other dietary elements are also necessary for growth, especially calcium, vitamin A and riboflavin (Sherman, 1941).

* "Food Consumption Levels," H M Stationery Office, 1944

CALCIUM AND BODY FUNCTIONS

Shortage of calories results in stunted growth also, as protein in such a case would be burnt as a body fuel instead of being used to build up the body. In the case of calcium shortage there would also be diminished growth in height, as calcium is necessary for skeletal growth (as are also phosphorus and vitamin D). Calcium has other uses beyond direct growth promotion, it is necessary for the absorption of food by the body (Magee and Sen, 1931), so in this way it might have a rather widespread bodily effect. It is also necessary for the contraction of the heart and arterial vessels and so for maintenance of the circulation.

But there is another function for calcium that is often forgotten, it helps the minute cilia of the respiratory and alimentary tracts to vibrate (at about 600 times per minute) and so keeps body fluids in motion in these parts of the body. In the nose, pharynx, trachea and bronchial tubes any interference with this movement of the cilia may prevent the proper cleansing of these mucous membranes, and this in turn may result in the onset of respiratory disease. Lack of calcium, of course, may also cause rickets, as with phosphorus and vitamin D it helps to form hard bone, and the type of rickets that may occur will depend upon the varying amounts of calcium, phosphorus and vitamin D. Sherman (1941) describes three different types, e.g., low phosphorus rickets and low calcium rickets and, when both calcium and phosphorus are short, an osteoporotic type.

THE VITAMINS

Sherman also states that any of these three types of rickets can be prevented by giving sufficient *vitamin D* unless the mineral supply is very deficient.

Vitamin A, if short, in addition to promoting growth and preventing night-blindness, also maintains (as does calcium) a healthy state of the mucous membranes. If deficient, the mucous membranes become cornified and the cilia may slough off, if this should occur, disease may be caused, not only in the alimentary and respiratory systems but even in the urinary tract with the formation of stone, and it was for this reason that parsley used to be given to prevent or cure stone in the kidney (see McCarrison's Cantor Lectures, 1936).

Shortage of *vitamin B₁* (thiamin) may not only result in beri-beri but may also cause mental depression, irritability and lack of mental concentration (Williams and Mason, 1941). Heart-block is another possibility.

If *niacin* (nicotinic acid) is lacking in association with other members of the vitamin B complex group, a pellagra-like condition may occur. In this country the symptoms may be sub-pellagral and may be readily overlooked.

Riboflavin (lactoflavin) deficiency is associated with angular stomatitis, seborrhoea, eczema, and perhaps vascularization of the cornea, and this condition is also likely to be overlooked in this country. The vitamin B complex group need to be in balanced quantity or deficiencies may occur. For instance, too much vitamin *B₁* may bring about riboflavin deficiency.

MINERALS

Among substances not scheduled in table 1 are sodium, iodine and, in trace amounts (Brockington, 1944), fluorine, zinc, copper and perhaps some other

minerals, such as manganese. Shortage of sodium may cause cramp, as sodium relaxes the heart and arterial and other muscles, iodine deficiency may result in goitre, and this may be prevented by one part of potassium iodide in 5,000 part salt, fluorine deficiency in dental decay, copper deficiency in anaemia and zinc deficiency possibly in interference with pancreatic function. The metals in trace quantities combined with protein may have an enzyme-like action but much research is yet needed to elucidate properly their action.

The necessity for balanced quantity of intake applies to minerals as well as vitamins, for instance, too much calcium may neutralize iodine and so tend to promote goitre, myxoedema, or cretinism, and sodium and potassium are antagonistic, especially in myasthenia, relatively more sodium being required in Addison's myasthenia and more potassium in myasthenia gravis. For these conditions the practitioner will have to regulate the amount of common salt (containing sodium) and vegetables (containing potassium).

GENERAL REMARKS

It is unnecessary to go through the whole gamut of dietary deficiencies, sufficient has been said to point out the need for an individual or group dietary survey when any nutritional deficiency is suspected, and in association with such a survey which would give the dietary food values, nutritional tests of the individual or group should be carried out somewhat on the lines mentioned at the beginning of this article. These surveys and the nutritional tests could be carried out by the medical officer of health, or his assistants, and for this purpose practitioners should notify or contact him, and medical officers of health, on their part, should make themselves acquainted with the procedure of investigations of this kind and also the statistical methods ancillary to them. On the other hand, if practitioners worked in groups at health centres, no doubt they also could carry through adequately such investigations, with clerical and statistical assistance. Work of this kind could be greatly accelerated by the establishment of special nutritional clinics, among the staff of which there should be a dietitian. The clinic should also work, and be linked, with the clinical research department of a university so that more complicated investigations could be adequately carried out, such as those relating to vitamin deficiencies.

Before concluding, another aspect of the question must be considered—the active promotion of good nutrition. This is a matter Sherman (1941) stresses very much in the concluding portion of his book, as does Lydia Roberts (1938). Among the things mentioned by the latter is the formation of nutrition classes for children, healthy habits (including dietetic habits).

Sherman points out how length of life could be extended by about 10 per cent and states that "the extra years, whatever the number may be, are not to be thought as added at the end of life but rather as an extension of the period of prime when both the individual realization of efficiency in accomplishment and the social value of one's services are highest." He speaks of "a much larger proportion of people getting such generous measure of buoyant health and capability for achievement as only the most fortunate few can now enjoy." The

diets suitable for promoting this extension of life and buoyant health are given. He advises the adoption of the scheme drawn up by Rose and Gray for child institutions in the United States, namely, take the percentages in diet as follows — from cereals 24 per cent, milk 32 per cent., dried legumes 1 per cent, other vegetables and fruit 16 per cent, fats and oils 12 per cent, meats, eggs and cheese 8 per cent., sugar and sweets 7 per cent., or, to put more briefly, take at least half the calories in fruit, vegetables and milk (including cheese and cream).

CONCLUSION

Nutrition work from the public health standpoint is something with which all practitioners should have something more than a nodding acquaintance, they should learn how to make use of the simpler methods of estimating nutritional deficiencies, sufficient at least to enable them to pass on certain patients for more detailed study, to others who have studied the subject more thoroughly. They should generally advise members of the public how important it is to adopt proper dietetic habits, and those interested should go further and take an active part in investigations regarding the nutritional state and dietary habits of their patients and the community in which they live. For if they do this then a buoyancy of health and extension of the prime of life may be attained that will add enormously to human happiness and human achievement.

References

- Abrahams, M, and Widdowson, E (1940) "Modern Dietary Treatment," London
 Bacharach, A. L, and Drummond, J (1940) *J chem. Ind*, 69, 37
 Brockington, F (1944) *Pub Hlth*, 58, 19
 Friend, G. E (1935) "The Schoolboy," Cambridge
 McCarrison, R. (1937) Lecture to Leeds Medical Society
 Magee, H. E., and Sen, K. C (1931) *Biochem J*, 25, 643
 Mann, C (1939) *J Clin Res*, 25, 85
 Mulligan, E. H. M (1945) *Med Off*, 73, 133
 —, and Fanning, E. Lewis (1942) *Ibid*, 67, 77
 Ministry of Health (1944) "Food Consumption Levels," London, H M Stationery Office
 Pyke, M (1945) "Manual of Nutrition," H M Stationery Office
 Orr, Sir J. B (1939) *J roy Inst. pub Hlth*, 2, 661
 Richards, Marion B (1945) *Brit med J*, 1, 433
 Roberts, Lydia J (1938) "Nutrition Work with Children," Chicago
 Sherman, H. C (1941) "The Chemistry of Food and Nutrition," London.
 Williams, R. O., and Mason, K. L (1941) *Proc Mayo Clin*, 16, 433

DIET AND THE SCHOOL CHILD

By R E SMITH, M B, F R C P

Medical Officer, Rugby School

CHILDREN to-day may go to a nursery school at the age of two and must go to an ordinary school at five, but often go when they are only four or perhaps three years old. These children have been given a real start in life, for healthy nutrition begins with conception. As soon as the mother realizes she is pregnant she gets, or can get, extra rations, and after the child is born she continues to receive these extras. Before the child is born she gets a pint of milk a day, three shell eggs a week, cod-liver oil or vitamin A and D, and concentrated orange juice; and after the child is born she gets for herself and the baby two pints of milk daily until the child is one year old, three shell eggs weekly for children from six to eighteen months, and cod-liver oil and concentrated orange juice. There are few mothers who do not take advantage of this scheme. When the child goes to school at the age of five he gets his third of a pint of milk in addition to the half pint he is allowed at home.

MILK AS THE SHEET-ANCHOR OF THE GOOD DIET

Milk plays the leading rôle in the diet of pre-school age and it is important to realize its value and its limitations. It contains fat, carbohydrate and protein, a certain amount of vitamins A and D and some vitamin C, and an easily assimilable form of calcium and phosphorus, but no iron. Milk should be prized chiefly for its protein and its mineral salts. The proteins in milk are caseinogen and lactalbumin which, when digested in the human or the calf's intestine, produce all the amino-acids necessary for growth and maintenance of the human or bovine body. A pint of milk contains 0.7 gm of calcium which, if taken daily, is sufficient to maintain healthy children in positive calcium balance. In the past, the value of milk has been judged chiefly for its cream content—a most fallacious criterion. Cream is of course useful, it is often an easily digestible fat, and has attached to it vitamin D, and it forms butter which is to the palate more pleasant than margarine which is made from vegetable fats, but it is completely wrong to consider that the principal use of milk is to produce cream. In fact, if the cream is separated, the skimmed milk contains the protein and the mineral salts, of which calcium and phosphorus, already mentioned, are the most important.

CALCIUM AND PHOSPHORUS

The Ministry of Food (Scientific Adviser's Division) in its recent pamphlet "Manual of Nutrition" gives the following figures for the calcium content of certain foods —

TABLE 1

	Mgm per oz.		Mgm. per oz.
Dried skim milk	348	Watercress	63
Cheese	230	Cabbage	18
Condensed milk	82	Turnip	16
Liquid milk	34	Cauliflower	14
Egg	17	Potato	2
Whitebait	240	White flour	5
Sardines	114	Bread	4*
Herring	28	Meat, most types	3
Cod	4		

* This figure was increased to 16 in 1942 by the addition of chalk to the national flour

This clearly shows that although skim milk has to be diluted ten times (1 pound of dried skimmed milk to 1 gallon, i.e., 10 pounds of water), it contains as much calcium as liquid milk. Education is required to convince the general public of the great value of skimmed milk. Nothing convinces some people better than figures. Table 2 below shows the percentage of the constituents in milk, cream and separated milk. Table 3 shows the caloric value of ordinary and separated milk.

TABLE 2

Percentage of	Milk	Cream	Separated Milk
Protein	3.4	2.5	3.4
Fat	3.4	40 to 50*	nil
Sugar	4.5	4.5	4.5
Calcium	0.14	0.1	0.12

* If obtained by skimming, the percentage may be about 20 per cent

TABLE 3

100 c.cm. = approximately 1/6 of a pint.			600 c.cm. is just over 1 pint.		
	No. of grammes in 1 pint of			No. of calories in 1 pint of	
	Ordinary milk	Separated milk	Caloric value	Ordinary milk	Separated milk
Protein	21	21.6	4.1	186	89
Fat	21	nil	9.3	195	—
Sugar	27	27	4.1	111	111
Calcium	0.84	0.72	nil		
			Total	392	200

These tables show that the caloric value of separated milk is half that of ordinary milk but separated milk contains protein, sugar and mineral salts in slightly higher proportions. As ordinary milk costs 4d-4½d a pint and separated milk when reconstituted just under 1d per pint (or 13s 1½d for a 21-pound drum), the housewife has a bargain. At the present moment when fats have been cut and it is necessary to save sugar for jam making, every housewife will find it helps

to use the top of the milk for fruit (gooseberries, currants, plums and apples). Fruit, when stewed or in a pie, with a little "cream" needs less sugar and children often prefer to drink the milk with the cream removed

Of the mineral salts in milk, calcium is the most important, and although 1 gm. of calcium is ideal for growing children, they are probably kept in good positive calcium balance with less, which is amply provided by their 5/6 pint of milk plus the extra in cheese (2 to 5 grammes per lb.) and in green vegetables. Phosphorus is also important, but fortunately if we take care of the calcium, the phosphorus will take care of itself. For 1 part of calcium, adults require 2 parts of phosphorus and children require 1 5 parts. This proportion is always maintained, as bread contains 40 mgm. per ounce, cheese 140, meat 70, egg 60, milk 27, vegetables 15 mgm. per ounce. If there is plenty of vitamin D present, the body easily adjusts the balance of calcium and phosphorus.

VITAMIN D

Calcium, phosphorus and vitamin D are necessary for healthy bones and teeth. They are like the three legs of a stool—no one of use without the other two. Vitamin D is found extensively in nature and can be made artificially, but the aim should be to make it for ourselves. Each child should have sufficient sunshine to make its own vitamin D for immediate use and for storage. It is common to curse the climate in England, but even in the worst month of the year, December, there is an average of one hour's sunlight daily. Every child should be exposed to the sun daily. Every child should have two weeks at the sea or in the country in the year. In this way he would make enough vitamin D to last him through winter. He can store vitamin D in his liver as easily as does the cod or halibut.

His advance in sociology will possibly be achieved within the next decade, and no-one will oppose this any more than they now oppose children's allowances, although these were bitterly opposed a few years ago. The habit of sensible sun bathing should be learnt in childhood and carried on into adult life.

THE IMPORTANCE OF WHOLEMEAL BREAD

Every child should be taught about good food. A simple experiment is to take a grain of wheat and cut it in its long axis so as to show the "germ" and the "bran." He should be told that if the bran is included the bread is brown. If the germ is included it is more or less the bread consumed at the present time and this bread is better because the germ contains some oil (which is fat in liquid form), iron and vitamin B and vitamin E and other substances capable of supporting life. The vitality of the germ should be proved to the children by cutting the grain into two, so that one half contains the germ and the other nothing but the white part which is starch, and planting the two halves, showing that the one with all these extra constituents will germinate whereas the starchy part does not contain the spark of life. Bread was called the staff of life long before milling removed the germ, science has shown that the germ is valuable, science has also taught the miller how to prevent wholemeal bread from becoming rancid. White bread may still be demanded by the ignorant, but that whiteness of bread should be regarded as a sign of purity is no more true than that a white-faced child is pure.

Wholemeal bread contains iron—the mineral salt essential for the construction of hæmoglobin, the pigment in the red blood cells. Anæmia is an all too common disease in England and several surveys have shown appallingly low percentages of hæmoglobin. It should be remembered that 100 per cent. hæmoglobin is the average, not the optimum. This can be illustrated best by an example of a much too infrequently described condition—health.

A well-built, thick-set boy, well above the average intelligence, first attracted my attention when he won the quarter-mile. He was in the XV. He weighed his food for a week in the holidays and ate 4,400 calories daily. His hæmoglobin was 120 per cent. He has since joined the Royal Navy and the last I heard of him was that he had been awarded the D S C for conspicuous bravery.

His hæmoglobin was 120 per cent. because he had ample choice in his diet of iron and protein, for the globin in hæmoglobin is important as well as the iron. Twelve others weighed their food and their hæmoglobins averaged over 100 per cent., the only boy with a figure below 100 being a food faddist. The point I am trying to make is that iron is in the food and that in bread and vegetables it is in a form easily assimilated. Girls need more iron than boys because they lose considerable amounts during menstruation. Every source should be tapped, and wholemeal bread is one.

It is difficult to make out a case for eating wholemeal bread for its vitamin B content. Pellagra and beri-beri were extreme rarities before the war, but every medical officer in a residential school marvels at the good health of boys and girls during the war, and attributes it to sensible feeding, and none advise reverting to white bread.

VITAMIN C

The usual foods supplying this vitamin have been in short supply during the war. Citrous fruits, oranges and lemons, are readily sought. Sensible people have included raw vegetables in their sources of vitamin C, but these are not popular with the majority of children, nor do some parents see any reason to take special measures against a disease—scurvy—which they have never seen and which none of their friends nor relatives have had. It was not always so. William Clowes (1540–1604) stated that he had seen twenty to thirty children with scurvy in the Blue Coat School (Christ's Hospital) at one time. The reasons for the change are numerous: the abolition of salted foods, the introduction of potatoes, the more regular use of green vegetables. This has abolished scurvy, that dread disease in which the blood vessels become like "perished rubber tubing" and there is bleeding from the gums, into bones and skin, and fractures and wounds fail to heal. There is to-day an increased tendency to bleed, to form large hæmatomas, and others think that superficial skin sepsis is prevalent because of lack of vitamin C.

Probably a minimum of 25 mgm. of vitamin C daily is necessary, and there is reputed to be 57 mgm. per oz. in blackcurrants, 28 in brussels sprouts, 20 in cauliflower, 20 in cabbage, 17 in watercress, 16 in orange, 14 in grapefruit, 12 in lemon, 8 in new potatoes, 4 in lettuce, 3 in onion and carrot, 1 in apple, plum and pear.

Potatoes are probably the most important single source. Cooking destroys some. It is important to cook only for the minimum time, to expose to air for the minimum, to use as little water as possible, and to use boiling water from the start.

GENERAL ARGUMENT

In discussing a particular article of food, it is easy to be led into by-ways and to neglect the main roads. For example, when wholemeal bread was discussed, I laid emphasis on it as a source of iron and neglected the animal sources, liver (the great storehouse of animals) and eggs. The fact is that all good foods are so well blended by nature that they contain the chief constituents of a good diet. That raises the question "What is the criterion of a good food?", the answer to which is "A good food is one which will support life." Milk falls into that category, but it must be remembered that the calf before it is many weeks old, indeed often when it is but a few days old, begins to eat grass to supply iron which is lacking in milk. An egg, if fertilized and incubated, will support life, but here there is also a fallacy because the developing chick absorbs 75 per cent of the shell to make its bones. A grain of wheat if placed in water will sprout and grow, although for proper fruition it requires ingredients from the soil, but if a few of these life-supporting foods are included in the diet—milk and dairy products (not despising skimmed milk), eggs and whole cereals—such diet will not want for much except vitamin C, of which there are good supplementary sources.

"All things work together for good" was a dictum often quoted by the late Professor Pembrey and which was inscribed on his tombstone. As yet not nearly enough is known about the interaction of various constituents of food. It is known that calcium without vitamin D is about as much good as gold is to the millionaire on a desert island, that carbohydrate is improperly metabolized in the absence of vitamin B, and thus beri-beri and pellagra arise, that insulin is necessary also for the combustion of sugar; but these are coarse mechanisms and there is yet much to learn about the delicate processes which are integral parts of human chemistry.

As science advances, it more and more justifies sensible habits. The child's longing for fruit, his frequent distaste for cream ("acidosis" was an early war casualty), his great demand for protein in the growing years of adolescence, are all supported by scientific data. The scientist has also shown that food to be really nutritious must be well cooked, and here let two caveats be entered—beware of food kept hot, especially meat soaked in gravy and, secondly, beware of dirt. Properly prepared food requires much labour, and this above all refers particularly to vegetables.

Diet is the basis of a sound nutrition, but the body and mind need training to lead the constituents into the right channels. Physical and mental education advance together. Parents are not willing to sacrifice physical health for scholastic prowess, nor usually is it necessary if every advantage is taken of the simple rules of health.

The breeding of healthy children is one of the national aims. Let it be realized that they are still children whether they be eighteen years of age at a public school, or twenty-one years of age in the Services, or fourteen onwards working in a factory. If the nation neglects the fourteen to twenty-one group, as they have in the past, the money spent in the years at school on mid-day meals, milk and medical and dental services is largely wasted.

In planning for the future, it is necessary to concentrate on vital foods. Fortunately this can be afforded by economizing on tea, alcohol and tobacco—useless materials from the health point of view.

COOKING AND THE NUTRITIONAL VALUE OF FOOD

By G NEIL JENKINS, M Sc, Ph D

Department of Physiology, St Bartholomew's Medical College

THE most obvious change brought about by cooking is in the appearance and flavour of food, and whilst this is often looked upon purely as an æsthetic matter, the great influence which these factors have on the appetite and on the secretion of the digestive juices must always be borne in mind. When feeding the sick, it is particularly important that methods of cooking should be adopted which improve the attractiveness of food, for, in addition to digestive considerations, it is usually true to say that those methods of preparing and cooking food which retain or improve flavour also retain the maximum nutritional value.

Before discussing in detail the influence of cooking on individual foods it may be as well to point out that all parasitic and many, but not all, bacterial infections are destroyed during cooking (Hutchison, 1940), although, of course, foods may be reinfected after cooking.

EFFECT OF COOKING ON DIGESTIBILITY

An important change occurring during the cooking of meat is the conversion of the tough collagen of connective tissue into soluble gelatin, which increases tenderness, facilitates mastication and consequently allows the digestive enzymes more rapid access to the protein. This change occurs more readily during stewing than in the application of dry heat and is increased by adding phosphate (0.2M phosphate between pH 6 and 7) to the cooking water, preferably in the form of concentrated stock from a previous boiling, which contains phosphates extracted from the meat. Another method by which tenderness may be improved is by the addition to a stew of vinegar, tomatoes or even sour cream which, by virtue of their acid, may accelerate the conversion of collagen to gelatin, quite apart from their contribution to flavour (Lowe, 1937).

Elastic tissue is virtually indigestible and is unaltered by cooking but fortunately in most cuts of meat the amount of collagen exceeds that of elastic fibre.

In contrast to this effect on the collagen of meat, cooking may cause a toughening of the actual muscle fibre, particularly with dry heat. These two opposing tendencies during cooking may explain why different observers have arrived at such contradictory conclusions about the effect of cooking on toughness. If the raw meat is tough because it contains much collagen, the breakdown of the latter during cooking may more than balance the increase in toughness of the muscle fibres, but if collagen is present in only small amounts then cooking may be expected to increase toughness.

It is commonly believed that when over-cooked, meat is less digestible than when underdone or raw but, whilst the time of digestion may be prolonged by over-cooking, it has been shown that digestion is eventually complete whatever the degree of cooking (Grindley *et al.*, 1907). It is widely believed, even in medical circles, that raw egg is easily digested. Beaumont found that raw egg passed through

the stomach rapidly but the reason for this was not, according to Van Slyke (1942), that the uncooked protein was rapidly digested but that it dissolved easily and hence was not retained by the stomach. The undigested raw albumen may actually be absorbed and cause a violent reaction, especially in infants. Van Slyke states that egg is most digestible when hard boiled and grated, although Andross (1940) found that lightly boiled egg was somewhat more readily digested than hard boiled, she did not compare either with the digestibility of raw. I can corroborate the view that raw egg is indigestible from my own experience.

Whilst acting as an experimental subject I ingested 100 gm of raw egg albumen daily for one week, followed by the same quantity of the cooked protein during the following week. Severe discomfort and very bulky faeces were produced during the first week, with a rapid return to normality during the second period on the cooked albumen.

The cooking of plant foods almost always improves their digestibility, by softening cellulose fibres and disrupting cell walls. The granules of uncooked starch, for example, are contained in a cellulose envelope which resists digestion by man, during cooking, the starch swells, bursts the envelope, and becomes free. The fibres and cell walls become softened and increase in permeability, and, although this might be expected to improve the availability of the soluble nutrients, the small amount of work that has been done on this point suggests that there is no difference between the utilization of vitamin C from raw cabbage and from a synthetic supplement (Clayton and Borden, 1943).

COOKING LOSSES FROM MEAT

Before discussing what losses do occur in the cooking of meat, it is important to dispose of a theory first put forward by Liebig and held uncritically for almost a century. This is the view that if meat is heated rapidly at first, an impervious "pellicle" is formed which prevents further loss of nutrients during the later stages of the cooking. McCance and Shipp (1933) first carried out the crucial experiment of comparing the losses of salts from meat cooked by plunging into hot water (when according to the theory the pellicle should be formed by the rapid coagulation of the superficial protein) and by gradually heating from cold. This experiment showed that the ultimate losses were identical and the initial losses were actually greater in the hot water. Although the theory must be regarded as quite untenable, it is mentioned, since it is still so frequently put forward. The only possible value in forming a layer of coagulated protein outside the meat is that the loss of melted fat may be reduced (Callow, 1945).

The most important cause of loss of nutrients from meat is due to the phenomenon of "shrink" which occurs whichever method of cooking is employed. When meat is heated above 60° C or so, it begins to lose weight and, since this occurs even if the meat is surrounded by water, it cannot be due to evaporation but is due to shrinking of the connective tissues, with a consequent expression of water and soluble materials. This process results in the loss of about 40 per cent of the total weight within two hours, when the temperature of cooking is 100° C, and is more rapid at the higher temperatures of pressure cooking. When the shrink is completed no further loss by this means occurs and the weight remains approximately constant, but when the meat is stewed or boiled, then, at least in small pieces (2 oz), the loss by diffusion may continue after the effects of shrink

have ceased. Diffusion may continue until equilibrium is reached between the meat and the cooking water, but as this takes up to six hours it is unlikely to occur in the course of ordinary cooking. When large pieces of meat (over $1\frac{1}{2}$ lb) were stewed it was found that after shrink was complete, smaller additional losses occurred by diffusion than with the size previously described. Apparently, the rate of diffusion of salts from the inside of the flesh was too slow to allow much of them to reach the surface. How serious is the loss of food value from these two causes, shrink and diffusion? The effect of shrink, uncomplicated by diffusion, was studied by measuring the losses during steaming. It was found that the loss of soluble salts approximately paralleled the loss of water, amounting to 40 per cent at the end of cooking; the loss of protein, although much smaller, was far from negligible, being about 5 per cent., and the non-protein nitrogen suffered losses up to about 30 per cent. Calcium, magnesium and iron, which are known to form complexes with protein, were found to be much less diffusible than the other minerals. The vitamins of the B group, although not studied by McCance and Shipp, would presumably be expressed like the soluble salts. The magnitude of these losses does not conform with the popular view on the value of steaming as a conservative method of cooking flesh, and indicates the desirability of utilizing the solution of extractives in gravies or in other ways.

When meat is *boiled* or *stewed* a greater proportion of the soluble constituents will actually leave the flesh than is lost in steaming or roasting, since, as already stated, diffusion takes place in addition to the active expression of materials during shrinkage, but in practice this is usually unimportant, as the liquid in which the meat has been cooked is consumed.

In *roasting* a somewhat different result was found. In the first place, owing to evaporation of water, the weight of the flesh continues to decrease as cooking proceeds, instead of remaining almost constant when shrink has ceased, as happens in stewing. Secondly, although the shrink will inevitably cause the expression of juice, when the latter reaches the surface of the meat the water will evaporate and the dissolved substances will be deposited on the outside. Only if the rate of expression exceeds the rate of evaporation will the juice drip off the meat with loss of extractives. This was proved by comparing the losses during roasting in a closed tin, when evaporation could not occur, with those when meat was roasted on open dishes. In the tin the losses were about three times as great as when the juice was able to lose its water and leave the soluble material on the meat. Open roasting may cause about 50 per cent. destruction of vitamin B₁ and riboflavin, since the evaporated juice is subjected to a high temperature for some hours (Mickelson *et al*, 1939). Fortunately, nicotinic acid, the only member of the B complex of which a large proportion of the daily intake is normally provided by meat, is very stable and undergoes no appreciable destruction, but may be lost by leaching or expression if the cooking liquors are rejected.

In *true frying*, in which food is fully immersed in hot fat, the losses of water are great, since the temperature of the fat is far above 100° C., but little material is extracted. Frequently fat enters the food with a corresponding increase in caloric value. It should be remembered that in this country much so-called frying consists merely of roasting with the food standing in a thin layer of fat, particularly in war time, when fat is short.

The final point to consider is the loss of fat. As the meat heats up the fat melts and a good deal will drip away, the loss being independent of shrink and evaporation. Typical figures given by McCance and Shipp suggest that 20 to 30 per cent. of the fat of a large piece of beef is lost in two hours' roasting or boiling, but the dripping so prepared is presumably used for other culinary purposes.

Much of what has been said about the cooking of meat applies to fish, the main difference found by McCance and Shipp was that shrink occurred to a smaller extent, but the loose texture permitted greater leaching.

Eggs and milk—This discussion of the cooking of protein foods may be concluded with a few words on eggs and milk. Hen's eggs (and also fish roe) contain proteins which do not undergo shrink and any losses incurred are due to extraction. Such losses have been found to be negligible during boiling or frying; even when poached in a large volume of water the salt loss amounted only to about 12 per cent. (McCance and Shipp, 1933) and the loss of protein 5 to 8 per cent. (Andross, 1940). The latter author states that about 13 per cent. of the protein is lost mechanically on cooking utensils when eggs are scrambled.

The boiling of milk coagulates the lactalbumin and along with calcium salts and fat forms the "skin" which contains between 10 and 15 per cent. of the total food value of the milk (Davis, 1944). This is a very real loss, as the amino-acids of albumin are necessary to supplement those of casein, and the loss of calcium should obviously be avoided. Children should therefore be encouraged to eat the skin, or, better still, its formation should be avoided by not heating the milk to a temperature higher than 70°C , which is warm enough for a hot drink yet lethal to all disease germs (Davis, 1944).

LOSSES IN VEGETABLE COOKING

McCance, Widdowson and Shackleton (1936) have summarized and extended early work on the mineral, starch and protein losses incurred in vegetable cookery. They point out that, although a high proportion of the minerals of vegetables may be extracted, the fraction of the day's requirements lost by this means is negligible. To quote their report. "Conservative methods of cooking vegetables are unlikely to increase the calcium, phosphorus and iron in a mixed diet by more than 3 per cent." Whilst it is clear that the vegetable cooking water may not contain nutritionally significant amounts of *minerals*, since so small a part of mineral requirements are satisfied by vegetable sources, a different emphasis must be given to vitamin C. In war time, vegetables are virtually the only constant source of this substance. Even in peace time, with a profusion of fruits of all kinds, surveys have shown that vegetables took first place as anti-scorbutics (Widdowson and Alington, 1941). It follows that excessive loss of this substance in the course of cooking cannot be viewed with complacency. Vitamin C may be lost or destroyed during the preparation and cooking of vegetables in three ways. First, many plants contain an enzyme, ascorbic acid oxidase, which causes a steady fall in their vitamin C content after harvesting. Cabbages, for example, lose about half their original vitamin C during one week's storage and old potatoes retain but one-fifth of that of the freshly dug tubers. Therefore, it is clear that vegetables should be consumed as soon after gathering as possible, because staleness involves more than merely a deterioration of flavour and crispness. This enzyme activity

increases if greens are bruised, and follows the usual acceleration at raised temperatures, hence careful storage in a cool place reduces loss by this process. When extensive cell damage of raw green vegetables is produced, for example by grating, contact between the enzyme and vitamin C is increased and considerable destruction may result. This is of no significance if the vegetable is used in small amounts merely as a flavouring (e.g., mint or parsley sauce), but such treatment should be avoided when a vegetable is a major constituent of a meal. There is no truth in the statement that vitamin C is destroyed by enzyme activity during the mastication of raw vegetables, an apparent loss certainly occurs but this has been shown to be mainly an experimental artifact and applies to the whole of the vitamin C of the diet and is not confined to that part provided by raw vegetables (Jenkins, 1944).

Boiling—When most green vegetables are cooked on a large scale it is important that they be plunged into boiling water small quantities at a time, so that the temperature of the water is never far below boiling point. By this technique, the rapid heating destroys the oxidase before it has time to oxidize appreciable amounts of vitamin C. In domestic cooking of cabbage, however, it makes little difference, and with other vegetables no difference, whether the initial temperature is high or low, since with a small pan, boiling point is reached so rapidly in any case (Lampitt *et al.*, 1943, Jenkins, unpublished).

The second way in which vitamin C may be lost in cooking is by extraction into the cooking water. This loss may be largely prevented, either by using a small volume of water, that is, by minimizing the extraction, or by using the water as a basis for soups and gravies. When cabbage is cooked the distribution of vitamin C between the vegetable and water often approaches equilibrium within the normal time of cooking, unless the vegetable is unusually tough. Thus if five times as much water as cabbage is used, then nearly five-sixths of the vitamin C will have diffused into the water within twenty to thirty minutes (Allen and Mapson, 1944). There is general agreement that the ratio of water to vegetable affects the retention of vitamin C and other soluble nutrients, although some workers have found a less striking effect than that of Allen and Mapson.

The Ministry of Food has widely publicized a method of conservative cooking which permits high retention of vitamin C, other soluble substances and, incidentally, of flavour in cabbages. The cabbage is quartered, shredded into strips about $\frac{1}{2}$ inch wide and added to a cupful of boiling salted water for each one to two pounds of vegetable, and virtually steamed for ten to fifteen minutes with the lid tightly on. The war-time difficulty of ill-fitting lids which do not prevent escape of steam may be met by a plate with a weight placed on it. It is a little sad to reflect that Englishmen have grown so accustomed to flavourless, over-cooked cabbage that many dislike it conservatively cooked because of the "strong" flavour!

Potatoes lose their vitamin C more slowly by leaching than do greens, owing to their smaller surface in relation to bulk, consequently, potato water is not a rich source of vitamin C or salts. Although the loss is slow it is progressive with time and if cooking—or mere soaking of the cooked potato—be prolonged, then the extraction may become considerable. The loss by root vegetables will be less with large pieces than with small, but since small pieces are cooked more rapidly, attempts to determine optimum size have been indecisive (Jenkins, unpublished). Extraction is reduced when the potatoes are boiled in their skins. Tightly packed

or fibrous vegetables, like brussels sprouts and cauliflower, are intermediate between cabbage and root vegetables in ease of extraction. A neat way of reducing cooking losses of potatoes is to boil cabbage and potatoes in the same pan. The vitamin C diffuses out of the cabbage, enters the water and, when the concentration exceeds that of the potato, no further diffusion occurs *out* of the potato, but a certain amount may actually enter, thus providing a cooked vegetable richer than the raw! A similar method of enriching a carrot consists of adding the green carrot-tops to the cooking water (Mapson, personal communication).

The third way in which the vitamin C content of cooked foods may fall is by irreversible oxidation during the process known, for want of a more elegant name, as "keeping hot". During the cooking itself the vegetable is surrounded by water which by excluding air keeps the actual destruction (as opposed to extraction) of vitamin C remarkably low, in occasional experiments it is *nil*. When the vegetable is removed from the water and kept hot, oxidation begins. Many factors influence the rate of destruction but it may be said that cabbage loses about half its vitamin C per hour under average conditions of keeping hot, and root vegetables in large pieces somewhat less (Olliver, 1941). If potatoes and root vegetables are mashed (i.e., thoroughly mixed with air) the rate of loss is about trebled. In fact it may be said that old potatoes mashed and kept hot for more than half an hour contain no more than traces of vitamin C, although the mashing itself, if carried out quickly, does not cause much loss (Lampitt *et al.*, 1943, Jenkins, 1943). If potatoes or roots must be kept hot they should be left whole, or in large pieces, and mashed immediately before serving. If bicarbonate is added to cooking water it does not increase losses of vitamin C during cooking (i.e., leaching) but greatly accelerates oxidation if the vegetable is kept hot (Olliver, 1941, Allen and Mapson, 1944).

Carbonate does cause destruction of vitamin B₁ and riboflavin, however, even during the boiling, although green vegetables are rarely important sources of these substances. To be on the safe side it is better to avoid bicarbonate.

In *steaming of vegetables*, extraction losses are negligible since shrink—which is responsible for the losses during the steaming of flesh—hardly occurs, but since the food is surrounded by air some oxidation of vitamin C occurs, the extent depending upon the duration of the steaming (Olliver, 1941). For roots, with which loss by extraction is small, even during boiling, steaming for the minimum time causes about the same loss as boiling; but if steaming is prolonged the loss is greater than in boiling. The careful steaming of greens is advantageous, since it avoids the major cause of loss in boiling, but again if prolonged may yield a product inferior to that resulting from boiling.

During *frying*, certain breakdown products of sugars are formed which interfere with the estimation of vitamin C and give spuriously high figures. Consequently many of the published results for vitamin C of fried foods are misleading. Using a method which avoids this error, I found that the average vitamin C loss in deep frying of chips is about 40 per cent of the original, but this is accompanied by so much loss of weight due to dehydration that the content in mgm per ounce remains practically unchanged. The caloric value of chipped potatoes may be as high as three times that of the raw, but this gain is not shared by roast whole potatoes. Two other gains which have been observed during vegetable cooking are in iron content from iron utensils and in calcium when hard water is used.

ow serious in practice are the losses of vitamin C? Recently I had the opportunity of analysing about 300 samples of home-cooked vegetables and found that average meal, if it contained a green vegetable and potatoes, and had not been t hot, provided between 20 and 30 mgm of vitamin C (30 mgm is regarded the desirable daily intake). When the second vegetable was carrots, or no nd vegetable was included, then the average meal contained about 15 mgm September and only 7 or 8 mgm in April (Jenkins, 1945). The lower figure the spring is due to the small contribution which old potatoes make compared th freshly dug ones in autumn. The loss of vitamin C in the domestic samples potatoes was fairly uniform at about 50 per cent of the raw value, which cannot regarded as excessive. Cabbage lost over 80 per cent on the average but with ich variation, the main fault in the cooking was the large volume of water e few housewives who followed the Ministry of Food's instructions served bbage up to three times as rich in vitamin C as the general average. It would seem m this survey that choice of menu (inclusion of greens) is at least as big a factor as the method of cooking in determining the vitamin C content of a meal. In communal meals the vitamin C tends to be low, especially in war time hen staff shortages may prevent satisfactory timing of cooking. With care, how- er, even communal meals may reach the target figure of 30 mgm, and many do

COOKING OF FRUITS

he cooking losses of fruits may be regarded as negligible, partly because the ater in which fruits are stewed is usually consumed, and partly because the acids esent stabilize vitamin C. The cooking of jam does not cause destruction of tamin C, but the addition of sugar and water reduces the concentration of the tamin to about one-third that of the original fruit (Olliver, 1940).

CONCLUSION

st it may be true that a generous, varied and peace-time dietary provides all utritional requirements however it is cooked, it is clear that with war-time hortages the employment of rational methods of cooking is important if the ximum food value is to be obtained.

References

- Allen, R. J. L., and Mapson, L. W. (1944) *J Soc chem Ind*, 63, 78.
 Andross, M. (1940) *Ibid*, 59, 449.
 Callow, A. B. (1945) "Cooking and Nutritive Value" Oxford, 31.
 Clayton, M. M., and Borden, R. A. (1943) *J Nutr*, 25, 349.
 Davis, J. G. (1944) *Food Manufacture*, 19, 385.
 Grindley, A. S., et al (1907) *Expt Sta Bull Wash*, 193.
 Hutchison, R. (1940) "Food and the Principles of Dietetics," 9th ed., London, 140.
 Jenkins, G. N. (1943) *Nature*, 151, 473.
 — (1944) *Biochem J*, 38, vii.
 — (1945) (In the press).
 Lampitt, L. H., Baker, L. C., and Parkinson, T. L. (1943) *J Soc chem Ind*, 62, 61.
 Lowe, B. (1937) "Experimental Cookery," 2nd ed., London, 223.
 McCance, R. A., and Shipp, H. L. (1933) *Med Res Coun Spec Rep Ser*, No 187.
 —, Widdowson, E. M., and Shackleton, L. R. B. (1936) *Ibid*, No 213.
 Mickelson, O., Waisman, H. A., and Elvehjem, C. A. (1939) *J Nutr*, 17, 269, 18, 517.
 Olliver, M. (1940) *Lancet*, 2, 190.
 — (1941) *Chem Ind*, 110, 586.
 Van Slyke, D. (1942) *Nature*, 149, 342.
 Widdowson, E. M., and Alington, B. K. (1941) *Lancet*, 2, 361.

THE HOSPITAL DIET

By RUTH PYBUS, OBE, SRN

Late Sister-Dietitian, Royal Infirmary, Edinburgh

THE science of nutrition is in its infancy but there is no doubt that scientific knowledge of dietetics is far ahead of its practical application. This can readily be understood in the feeding of the nation as a whole, for it is a stupendous task to teach the masses even the simplest principles of a well-balanced diet, to break down food prejudices, to produce sufficient food and, above all, to see that an adequate diet is within the purchasing power of the poorest section of the community. In the face of a world shortage of food such a problem would seem almost insoluble. No-one will deny that food at present is monotonous and that it falls short of the ideal from a nutritive standpoint. But it is to the credit of this country that, in spite of a world war, for the first time in history a national diet has been planned which is based upon the nutritional needs of the people. Is it possible to say that the feeding of the patients and staff in the majority of hospitals has been planned on an equally scientific basis? Much valuable research in dietetics has been carried out in the laboratories and wards of the leading hospitals but until recently there has been little attempt to plan the hospital diet in the light of this newer knowledge of nutrition.

During the past few years many hospital committees have been vaguely conscious that all was not well in their catering departments, and the more enterprising hospitals have initiated a dietetic inquiry and have discussed the best means of overcoming the defects which these surveys have revealed. In July 1943 the King Edward's Hospital Fund for London published a memorandum on "Hospital Diet," including a detailed analysis of the meals at three hospitals in the greater London area. The report indicated that, whilst the results of these surveys did not justify general statements regarding the adequacy or inadequacy of hospital diets, the position which was revealed by the investigation was disturbing and showed that the diets both of patients and of staff may sometimes be seriously defective, judged by modern nutritional standards. These findings have unfortunately been confirmed by other dietary surveys in different parts of the country. Not only are dietary essentials frequently deficient but the food is often lacking in variety, it is insipid in flavour and unattractive to look at. It is not too much to say that in some cases the recovery of the patient is hindered by this inadequate and unattractive food. The nurses' diet is usually more plentiful and more varied but even in peace time there is often a preponderance of "stodgy" dishes with a poor supply of fresh fruit and vegetables.

DIETARY STANDARDS

Hospital dietary surveys frequently give a wrong impression of the adequacy of the food which is provided, and the responsible authorities may be lulled into a sense of false security because the amount of nutrients is reasonably in accordance with the supposed standard requirements.

Calories—It is not sufficiently appreciated that the theoretical caloric require-

ent for "bed rest," or for the sedentary man, makes no allowance for the increased metabolic rate in fevers, for the extra nourishment which is required by the patient who is convalescing from an acute infection, or for one who is fighting against a long drawn out and debilitating illness. No "average" caloric requirement can be fixed in cases of acute illness and the patient's powers of digestive assimilation must be considered. Perhaps there is a tendency to overfeed the patient in cases of acute disease of short duration, but the hospital diet is almost always inadequate for those patients requiring hospital treatment for many weeks. The monotony of the diet is an important factor in such cases and this is a common cause of a sub-caloric intake, resulting in loss of weight. Physicians should not only demand a check of the caloric intake of their patients but they should insist on a reasonable variety and choice of food. In surgical wards the number of calories provided for a few days may be of little importance in the case of a well-nourished man, but the poor diets which are often given to debilitated patients, the inadequate calories provided in the older methods of tube feeding, the small amount of food which can be taken by the patient with a jaw injury—all these and any other cases might show a more rapid rate of recovery if the surgeon insisted on a nourishing diet prepared in a suitable form. A high caloric diet is difficult in war time, but it is not uncommon to find that the special rations which are authorized for such patients are not being ordered by the medical officer or supplied by the house-steward or housekeeper.

Protein—The standard figures which are often accepted as the protein requirement for the hospital patient are particularly misleading. It is believed that 1 gm. of protein per kgm. of body weight is more than enough to maintain nitrogen equilibrium and to prevent symptoms of protein deficiency in the healthy adult (although incidentally this figure seldom allows for a satisfactory and varied diet). In cases of illness this modest figure for protein may be inadequate, for a sick man cannot derive sufficient calories from the bulky carbohydrate foods which prevail on the war-time diet, and his allowance of sugar and fats can only be increased at the expense of that of other patients. Moreover, there are many conditions in which generous protein feeding is desirable—for example, in cases of burns, tuberculosis, hypoproteinæmia, pregnancy and lactation. In pregnancy, not less than $1\frac{1}{2}$ gm. of protein per kgm. of body weight should be provided. In many hospital diets which have been analysed the protein is inadequate, whilst in others it appears to be generous, but a closer scrutiny will show that, in many cases, the animal protein is almost all derived from milk and that the only cooked "protein" meal is provided at dinner. The breakfast, tea and supper may consist almost entirely of tea and bread and butter or margarine, together with any extras supplied by the patients' friends. Most hospitals are now endeavouring to serve an evening meal and many are also providing a cooked breakfast for patients who desire it. This additional expense is entirely justifiable. The supply of milk in most hospitals is fairly generous, even in war time, and because of this the animal protein compares favourably with that of the rest of the community. Nevertheless, it is a mistake to rely so much upon one commodity, especially in war time, when the milk supply is uncertain. Milk, although an excellent source of protein, calcium, phosphorus and riboflavin, is particularly poor in iron and is almost devoid of vitamin C. A plate of fish or meat or egg with a salad or properly cooked

vegetable would make up for these deficiencies. It is usually found that in hospitals which do not provide a cooked protein meal in the evening the patients do not receive all their rations or "points foods," and they may become hungry before breakfast. Besides, from the physiological viewpoint it is better to distribute the protein more evenly throughout the day. It should be realized that in a large hospital an extra cooked meal will involve an expenditure of several thousands of pounds annually, entailing as it does extra food, equipment, cooks and porters. No hospital committee will grudge the additional expenditure for the benefit of the patient, but the present position regarding shortage of staff and equipment is a serious problem and it is undoubtedly hindering reforms in hospital feeding.

Mineral salts—In the consideration of a diet the calcium, phosphorus and iron are the only mineral elements which need receive special attention, for if these minerals are present in satisfactory amounts the others will also be well represented. The figures shown in dietary surveys often give a false impression of the adequacy of calcium and phosphorus, for if these minerals are derived chiefly from oatmeal and other whole grains much less will be utilized than if they are supplied from dairy produce—milk, cheese and eggs. The bran of cereals contains much of the phosphorus in the form of phytic acid, and this combines with calcium to form insoluble calcium salts. For this reason, and because of the shortage of milk, a small quantity of calcium has been added to the national loaf. It is not suggested, however, that the national loaf should replace milk and cheese as a source of calcium. The calcium content of cooked vegetables depends greatly upon the calcium content of the water in which they are cooked. This is particularly true of potatoes, which are rather poor in calcium. It may be accepted that if the milk in the hospital diet averages one pint per head and if cheese is used the calcium and phosphorus will be excellent. If less than half a pint of milk is provided these minerals are almost always deficient. In maternity hospitals a special check must be kept on the amount of milk supplied. In this respect the patient is sometimes better off in her own home than she is in hospital. In a busy ward the administration of the vitamin concentrates may also be overlooked.

On one occasion a young woman was visited in her home soon after she had been discharged from a maternity hospital. She was full of the kindness and skill of the medical staff and nurses but she remarked innocently "Now I am home I think I shall get my strength up and be able to nurse my baby, because I can get the right food. You can't expect a hospital to afford a nourishing diet for all those patients!"

The iron in the hospital diet to-day is probably higher than it was before the war, when most hospitals served white bread to both patients and staff. The iron content of oatmeal and brown bread is particularly useful and the increased consumption of vegetables in some hospitals has also helped. Eggs are a valuable source of iron but, even in peace time, some hospitals only provided eggs for patients on "light" diets and others had to rely on the generosity of their friends. A chemical analysis of the iron content of an institutional diet shows great variation from day to day. Dr. Pyke, of the Ministry of Food, found on one occasion that 76 mgm. of iron were present when apple tart was served to the nurses. Apples, being an acid fruit, readily pick up iron from kitchen utensils. Such an uncertain source of iron should, of course, not be relied upon. The iron content of the nurses' and maids' diet is of particular importance and an intake of 15 mgm.

uld be aimed at. If this generous figure is taken as a standard, the sources the "availability" of the food-iron need not receive special consideration. The use of dried eggs, oatmeal, pulses, dried fruit and green vegetables should be included, together with the meat ration and liver, when it is obtainable.

Vitamins—The provision of adequate amounts of certain of the vitamins is one of the major problems in institutional feeding, and dietary surveys have shown that in many cases it has been the custom to rely upon the patient's friends for the supply of such "protective" foods as butter, eggs, tomatoes and fresh fruit. The amount of the different vitamins which can be given with advantage to maintain a maximum degree of health, vigour and resistance to disease is not known, and it is a mistaken idea to assume that the requirements for all men are the same. Even in health there is a variation in the individual's ability to make use of the vitamins and pro-vitamins which are present in the diet.

The hospital patient requires a generous supply of vitamins, for he has often had a poor diet before admission to the ward and his reserves are therefore low. Frequently the powers of absorption are impaired by gastro-intestinal disturbances, and by the administration of medicines. The requirements for certain vitamins are increased by fever, infections, the processes involved in the healing of fractures and the repair of wounds, and by various metabolic disorders. The physician or surgeon does not always appreciate these facts, nor does he realize the extremely poor supply of vitamins in the average hospital diet. Under existing conditions of cooking and food-service, and with the limited supply of fresh fruit and dairy produce, it is difficult to reach ideal standards, and in certain cases the administration of vitamin concentrates is essential. It should be realized that some "multiple" vitamin preparations contain inadequate amounts of some of the substances mentioned on the label and it is poor therapeutics to rely on pills and capsules and to provide a badly balanced diet. All the vitamin concentrates on the market may fail to include some of the less well-known, but no less important, dietary factors, whilst fresh fruit and vegetables and dairy produce provide not only vitamins but many other valuable dietary essentials. A pint of milk, two servings of fresh vegetables, a salad or citrus fruit, a good serving of meat or fish, the full use of the fat ration and all available fatty fish, cheese, fresh and dried eggs and liver, a generous supply of potatoes and the inclusion of brown bread, should form the basis of the "protective diet."

Unfortunately, the methods used in institutional cooking may seriously affect the natural vitamin content of food. Vitamin A withstands ordinary methods of cooking but may be partially destroyed by overcooking. Thiamin (vitamin B₁) is destroyed by pressure cooking, by the addition of baking powder or other alkalies sometimes used in baking, and there is some seepage into the vegetable water. The B₂ group of vitamins is more stable. Vitamin C (ascorbic acid) is sometimes completely destroyed before the vegetable or potatoes reach the patient and they cannot be relied upon as the sole source of ascorbic acid. Besides, the vitamin C content of different fruits and vegetables is so variable that it is possible to take considerable quantities of such foods and yet be short of this vitamin. Lack of space prevents a description of the destruction of vitamin C during the preparation and serving of food, but satisfactory results can only be obtained if the vegetables are cooked briskly for a very short period in a small amount of water,

if they are used soon after they are gathered and if they are served immediately after cooking. The difficulties in institutional cookery are manifold and the necessity of conveying food to the wards in heated containers makes it obvious that cooked greens and potatoes are a very uncertain source of vitamin C in hospital diet.

ADMINISTRATION

Much has been written lately about the necessity for a complete re-organization of the hospital food service, and there is no doubt that some reform is long overdue. Sweeping statements are, however, unjustifiable and there is a wide variation in the quality and quantity of the food which is provided, and in the methods of its preparation and service in different hospitals. There is also a great difference in the consideration which is given to dietary requirements and in the facilities which are available for the service of "special diets."

It is unfortunate that the effort to improve the hospital diet coincides with the most difficult period and, owing to a shortage of labour, equipment and food, it will probably be some years before ideal conditions can be attained. In the meantime certain improvements can be aimed at.—(1) The hospitals must be prepared to pay sufficiently high salaries to attract the best type of food-supervisor and a staff of well-trained cooks. The status and living conditions of the food supervisor or dietitian might also be improved. (2) A great effort should be made to train more dietitians and to give them good experience in catering, large-scale cookery and administration. Eventually all the "food service" of the hospital should be under the supervision of a dietitian-caterer. (3) The meals of the staff should receive more consideration. This would prove an additional incentive to women to take up nursing, and it might well result in a decrease in sickness amongst the nurses. (4) A dietary survey should be carried out at regular intervals and attention should be paid to the standard of cooking and the variety of the food as well as to the nutritive value. Those hospitals which cannot secure the services of a full-time dietitian can ask for the advice of the experts employed by the King Edward's Hospital Fund or the Ministry of Health. (5) Special consideration should be given to "light" diets which are often needlessly monotonous and lacking in "protective foods" other than milk. (6) Under the rationing scheme care must be taken to see that patients receive their full rations and that the staff or private patients are not fed at the expense of the ward patient. (7) The facilities for serving "special diets" should be improved in many hospitals. (8) The setting up of a permanent food committee should be considered. This might be comprised of the medical superintendent or secretary, the matron, dietitian, house steward, and a member of the honorary medical staff and of the house committee. (9) Dietitians should be requested to give lecture-demonstrations to medical students as well as to nurses in training.

It has been truly said that "the food service should be regarded as one of the essential remedial services offered by the hospitals." The necessary improvements in hospital feeding can only be achieved by the support and cooperation of the whole of the honorary medical and surgical staff, together with that of the most junior house physician. No hospital committee will feel justified in increasing expenditure on food unless it is backed by the medical staff. The dietitian also needs the encouragement and guidance of the medical profession.

SLEEP IN HEALTH AND IN ILLNESS

By S WATSON SMITH, M.D., F.R.C.P.

*Consulting Physician, the Royal Victoria and West Hants Hospital, Bournemouth**"that sweet sleep
Which thou ow'st yesterday"*

ANY words have been bandied as to the amount of sleep needed at the recent ages, but who can fix this, an admitted variable, better than the person, and then only vaguely? The function of rhythmic sleep is so hedged round and controlled by factors subject to every variation that, after all, each becomes a law unto himself in the matter, which perhaps is regulated most by fatigue and nocturnal habit. The hours of natural sleep cannot be constant, must vary and fluctuate from night to night according to state of health, itself a static quantity, to expenditure of energy, besides various other circumstances yet the approximate hours prescribed would almost seem to be set, arbitrarily, for each age-group. The controversy over the measured allowance of sleep in schools is never-ending, probably because there can be no end to it anything, it errs in being insufficient. However, it appears to be generally conceded that the figures offered by Dr Clement Dukes ("Health at School," 1905) are right, or nearly right, namely:—

"Under 6 years of age, 13 hours, from 6 p.m. to 7 a.m., under 10 years of age, 11 hours, 3 p.m. to 7 a.m., under 15 years, 10 hours, 9 p.m. to 7 a.m., under 17 years, 9½ hours, 3 p.m. to 7 a.m., under 19 years of age, 9 hours, 10 p.m. to 7 a.m. From the beginning of November to the end of February, the length of time should be extended to 7 30 a.m."

These figures can be accepted for boys and girls, whether at school or at home from puberty to full development—sixteen to twenty-five years—eight hours is many thought to be enough, yet, at this period of life perhaps the greatest daily expenditure of energy is made, to recover from which longer sleep should be required so that nine or nine-and-a-half hours lies near the mark. The need for sleep during the years of adolescence goes without saying.

The infant sleeps the greater part of the twenty-four hours, waking only to be nursed and fed, the young child sleeps during more than half the twenty-four hours of the day; the older child sleeps about twelve hours. On the average, the adult sleep varies between eight hours for the physical and ten for the brain worker; although a few seem to be satisfied with six or seven hours' sleep, fewer still with five, and a few declared four to five hours in bed. If this last be true, is it because the hero of the shorter hours "toils not neither does he spin," so conserving strength and energy? Whether this brief rest fulfils the whole natural need or happens except in short intervals is doubtful, to say the least. When a statement like this is ventured, it will be accepted with some misdoubt, for none knows but fallibly how long and how deeply he or she sleeps, few how much or how little restorative sleep is actually needed in their particular case.

The quality of a man's work, as well as his frame of mind, depends greatly upon the measure of his night's rest. Whereas one who sleeps well, works well, he who sleeps badly will live a poor life and do a laborious and burdensome day's work. With hours of sleep that are stunted and irregular, skill and proficiency suffer,

to become impaired and reduced. This is noticeable in the night worker who to seek his hours of sleep in the day-time, too often in a noisy, unrestful environment. Whether in factory or institution, an inverted rhythm of work and sleep cannot be maintained for more than about five months, at the most, without loss of efficiency and health. Overwork, on the other hand, requires sleep enough to compensate, which it will do partially and for a time only. It is certain that those exceptional people having no leisure time, who occupy with intensive thought and active toil every minute of the day, are unquestionably in greatest need of sound sleep. No member of the community, of whatever occupation, can compare in hours of work—in time and anxiety—with the busy men and women practitioners of medicine, who labour steadily and continuously, without complaint a daily day, commonly of sixteen or seventeen hours—double the average length of the working day—so being too often denied the necessary amount of recuperative sleep. The pressing nature of medical practice makes a fair night's rest unattainable.

Loss of sleep occurs of all degrees, partial to complete, varying in depth as well as in length. Whereas the light sleeper may sleep all night, another will sleep only to wake in the early hours to sleep no more, and there are those who lie awake until early morning, then sleep late. The more harmful type of insomnia is that in which the individual awakens in the early morning hours to lie awake for the rest of the night.

Disturbances of the rhythm of sleep are met with. In some, these are encouraged by the habit of the afternoon nap which spoils the night's rest. To become by night-time physically and mentally tired is the most natural thing in the world without which sound sleep is hardly to be expected. In the healthy, lack of exercise disposes to insomnia. It is a provision of nature that tiredness demands and requires restorative sleep during hours of darkness "when no man can work."

In the otherwise healthy, prolonged insomnia demoralizes and exhausts, in the sick, it may prevent recovery, and will even destroy life if not met promptly and well. In childhood, feebleness of mind and body usually results in disturbed rest which, however, needs not drugs but the teaching of a regular habit of sleep. In disease, epidemic encephalitis is the outstanding cause of reversed or inverted sleep rhythm, the sufferer sleeping in the day-time to be awake all night.

MANAGEMENT OF THE SLEEPLESS

DORMITIVE TREATMENT—To encourage sleep, whether in health or sickness the bedroom chosen should be quiet and noiseless, capable of being completely darkened. In health, the temperature of the room should not exceed 56° F. in illness a steady temperature of 60° F., and not higher than 65° F., ought to be maintained. The less the furniture and the fewer the furnishings, the better. If there is any choice in the matter of the bed itself, this ought to be a single one with spring mattress, placed in the middle of the room to allow of easy access from all sides, the head of the bed towards the window. The fear of draughts is real to many; these are only likely to be harmful if felt, but can be avoided and good ventilation secured in all weathers, at all seasons, by placing a 4- or 5-inch block of wood, accurately fitting, under the raised lower sash of the window. If an open casement, this may have to be screened, or a looped pad suspended

both door handles to hold the door ajar so as to compensate for the closed window in bad weather. A suitably placed screen will counter draughts from the window or door to fireplace. The bed-covering should be light, never too bulky, blankets and sheets being safety-pinned together. A good nurse knows well even the pillow must be of the correct height and comfortably adjusted. To prevent skin burns, all hot-water bottles should be covered—an inviolable rule removed altogether from the bed when morphine or an hypnotic drug has been administered.

Posture in sleep is important. the natural, so-called prenatal, position, on one side the other, with all limbs fully flexed, is the correct one, most choose to lie on the right side, a few on the left. It is peculiar that in known prehistoric Saxon times this position was usual, as if in imitation of the living sleeper. In a children's school, this posture is the common one, and they, more than adults, are prone to lie down under the bed-covers for extra warmth perhaps and to silence of all sounds. Thereby, they re-breathe their own used air with its carbon dioxide content, to sleep more deeply, yet appear to suffer no ill-consequence.

The snorer with an ample air-way always snores because he lies flat on the back. The oral snore is caused by the uvula and soft palate flapping back against the pharyngeal wall, sometimes by the tongue and mandible dropping backwards, a nasal snore arises from flapping of the alæ nasi, or from obstruction of the nostrils from other cause. Obstructed breathing thus provoked is inspiratory, never expiratory. There are, however, some individuals, healthy enough, who snore furiously and loudly whatever their posture in bed, yet refuse to admit to so much, how to cure them, or indeed how to deal with them other than by segregation is difficult to know.

Incidentally, the patient in *coma* from whatever cause, allowed to lie supine, sometimes takes this oral or nasal snore which, if happening in the night, intensifies the nervous tension felt by onlooking relatives. The silence can be felt when the practitioner, arriving by the bedside, quietly turns the patient's head to one side to stop the snore. If comatose and too heavy to move readily, then all that is necessary is to place a pillow under one shoulder to keep the head turned towards the opposite side. When a nasal snore is caused by inspiratory indrawing of the alæ nasi, this can be stopped and the air-way kept wide open by inserting a half-inch strip from the end of a calling card, rolled round a thermometer case, and slipped horizontally along the floor of each nostril, the free end being allowed to project beyond the external nares for easy replacement.

In *semi-coma*, restless sleep may result from retention of urine. An over-distended bladder should be relieved without delay, and catheterization patiently repeated by means of a soft rubber catheter every six or eight hours, an attention not to be postponed or neglected if overflow and an atonic bladder are to be avoided, as well as much pain and discomfort to the patient.

Cramp in the calves and feet may cause much dreaded pain to the sufferer; this is speedily overcome by placing a board across the foot of the bed against which the foot is pressed firmly. Although preventive medicinal treatment for cramp is often given, this is usually a failure, and is unnecessary if a foot-board is utilized to prevent or stop the cramp the moment this makes itself felt.

Although *cold feet* will prevent sleep, this is easily countered, hot feet are different problem. Fiercely hot feet are a rarer complaint, a disability not readily rectified by a cold-water bottle or analgesic drug.

THE SIMPLE REMEDY—To encourage sleep, the usual first means is the hot drink of a non-stimulating kind at bedtime. In the elderly, whisky with water and sugar may be habitual, and should not be vetoed lightly in those below the age of sixty years. Amongst medical men who notoriously sleep "with one eye open," it is a better plan to eschew hypnotics and to depend upon the prospect of getting out of bed and boiling a simple drink to take before tumbling into bed again. This is an infallible remedy in the case of a busy colleague of mine.

Apart from the bedtime drink to invite sleep, no fluid should be taken within one-and-a-half hours of going to bed, and no full meal within three hours. A quickly filling bladder that has to be evacuated oftener than twice or thrice in the night, or a stomach too full, will ruin a night's rest.

The mind-quietening, nodding effect of the bedside book should not be disregarded. The best at the moment is J. B. Firth's *Miscellany*, or *The Bedside Book* by Arthur Stanley.

Hypnotism, these days practised by the few, can have success in very few patients, and those chiefly with mild functional nervous conditions. Nowadays the method, because of its past shortcomings, is not taken seriously by the practitioner of medicine, being supplanted by other, better means.

SOPORIFIC DRUGS—Because of the hurry and excitement of present-day living, with the consequent increase in nervous tension for many, perhaps because of the various day and night noises, there is greater demand for, and need of, night sedatives and hypnotic drugs. Many of the older of these, such as the sulphones and carbamates, and even the bromides, are being superseded by new drugs, and now live only in the bypaths, as it were, paraldehyde, chloral and morphine, of continued good repute, and the more recent barbiturates, hold their pride of place. Combinations of these are commonly employed, with small amounts of bromide, opium or hyoscine added, these mixtures being found of greater benefit at the bedside. In clinical practice, the hypnotics of real helpfulness are a chosen few. The greater success follows the medical man who knows how to employ them in good time, with thought and care, and when to withhold the hypnotic after pain is controlled, and a drugless sleep should be encouraged. Morphine continues to stand by itself above all its many derivatives (which are actually more pain-killers than hypnotic) in spite of its several disadvantages, as the best drug to count pain, being the more useful because of its hypnotic qualities. Used with select discrimination, it cannot be displaced as the ideal drug in certain cases and circumstances, although never to be made use of before diagnosis is confirmed for fear of masking and beclouding this by dispelling pain which, after all, has its beneficent warning aspect. If formerly, morphine and the opiates were freely misused perhaps the pendulum has swung over too far, and a dread of its being wrongly applied may prevent its better employment, particularly so now that many new hypnotic drugs, or combinations of the old and new amongst these, are available.

Whether prescribing chloral or a barbiturate or morphine, three precautions are advisable—to fix and check dosage, to limit the quantity ordered, and to

the giving to a nurse or other who will keep the preparation under lock and key. At times, importunate demands for an opiate or for a favoured barbiturate are made by a patient not in real need. It is necessary to be firm in refusal, and careful in substituting some drug less potent for harm. Whichever is resorted to, given in the interests of the patient, who may not always appreciate the denial of the self-chosen unsuitable, if favourite, drug.

(1) *The bromides*—Although the bromides of potassium, sodium and ammonium, as nervous-system depressants, they are, apart from frequent employment in sick children and infants and sparing use in adults, seldom prescribed alone, having been generally replaced by barbiturates. Probably the reason for this is that bromides are cumulative and toxic in repeated, even small, dosage, because elimination by the kidneys lags, being too slow. Then, again, their sedative effect is of greater use than their hypnotic action. With prolonged use, the bromides can seriously dull the mind. In these days, they are chiefly used combined with other drugs—chloral hydrate or a barbiturate—in the treatment of insomnia brought about by worry and anxiety. Of the three salts, when used alone for the purpose of securing sleep, perhaps the most effective is the unpalatable ammonium bromide, grains 15 to 30, as an adult bedtime dose. In secondary insomnia, such as is caused by anxiety, the dilute hydrobromic acid B.P. (15 to 60 minims) is of use, and in secondary thyrotoxicosis, quinine hydrobromide B.P.C. (grains 1 to 10), in mixture, is helpful in quietening nervous excitement and in preparing the patient for sleep, assisted by a barbiturate given at bedtime. Poisoning by bromide is not lethal. It takes the form of bromide acne, a papular and papulo-pustular eruption of the face and upper back, or a pustulosis occurring in infants and young children in the shape of plaques on the body or limbs, and depressed, slowed actions with mental deterioration, either or both being more apt to occur when bromides in small amounts have been continued for any length of time.

(2) *The halogen derivatives*—Of these, chloral hydrate B.P. (grains 5 to 20) is mostly used, and for all ages. This acts speedily, producing drowsiness in fifteen minutes and, within the hour, sound restful sleep that lasts for six or eight hours, leaving behind no depressing effect. Chloral hypnosis is not at any time so deep that the patient cannot be roused out of it. In the past, the drug was given a bad name, being believed to be harmful and unsafe, particularly in those with heart disease. In many years of practice, I cannot recollect any instance of mishap ensuing, although the drug was utilized in many patients, even in those with cardiac degeneration. It is possible, indeed likely, that harm had followed its use in too great quantity, as would follow overdosage with almost any drug.

Commonly, the hydrate is combined with either potassium or sodium bromide, to supplement the effect. Alone, or thus combined, no hypnotic is more reliable or safe in correct doses, although inadequate or failing when there is pain, in which case tincture of opium or the sedative solution of opium B.P.C., 10 or 15 minims, can be added to each dose with good effect. This mixture

R. Chloral hydrate	10 grains
Potassium bromide	10 or 15 grains
Sedative solution of opium	10 or 15 minims
Syrup of orange	60 minims
Chloroform water	to $\frac{1}{2}$ ounce

In time, the barbiturate habit causes even a sharp-minded, intellectual person to be forgetful, stupid and slovenly in a surprising way, this is not always discible except in an old friend or client—in "an old struggler" with the habit—wh previous high mental attributes can be recalled

It is a wise plan in the case of the depressed, unhappy individual, per silently obsessed with thoughts of persecution, to withhold the prescription a barbiturate or the dispensed tablets themselves, placing these in charge of another who will dole out the dose at the correct time, strictly in accord with the practitioner's directions, the hour of administration and amount being written up and charted. A barbiturate in tablet or capsule form is too easy and handy for a drug taker or the suicide. There is much to be argued against self-administration of drugs of the barbiturate group, or indeed of any hypnotic medicine whatsoever.

(5) *Opium and morphine*—When insomnia has pain as its cause, or paroxysmal cardiac dyspnoea, morphine hydrochloride (dose $1/8$ to $1/3$ of a grain), hypodermically, is both prompt and effective in relief, and cannot be bettered by any of the pain-killing opium or morphine substitutes or derivatives. Morphine is the best of the whole series in its combined pain-relieving and hypnotic action for proper occasions only, and these in practice are few. By mouth, tincture of opium (laudanum), dose 5 to 30 minims, will control most pains, being in practice given with chloral hydrate, as previously described, to secure the double action. A favourite alternative to laudanum thus used is the sedative solution of opium B.P.C. (dose 10 to 30 minims). Initial doses of either morphine or opium should be minimal. With tolerance, the dose has to be increased in amount, although this should seldom be allowable, or indeed necessary, when other, more suitable hypnotics are now available to continue with. In chronic sleeplessness, it is better practice to allow morphine or opium at all. In many cases, if pain is removed, natural sleep will follow. It is here that an opium derivative has a judicious use. Repeating a bedtime dose of morphine for more than a day or two at the start of an acute illness is usually unnecessary, it should then be withheld, some other drug less potentially harmful being prescribed. In pneumonia, for example, it is recognized as wrong practice to continue morphine beyond the third night of disease at the latest, its use here is to control the stabbing pleuritic pain and mental distress which so often initiate the illness, thereby, and at the same time inducing the added sleep-producing, "morphan" effect of the drug. In employing morphine, because of its known contrary action as a circulatory and respiratory depressant, either strychnine hydrochloride $1/60$ grain, or nikethamide (see Addendum III), 3 to 8 grains, can be added, if need be, to counter this unwelcome effect and to fortify the patient.

(6) *Henbane*—Hyoscine hydrobromide B.P. (dose $1/200$ to $1/100$ grain), is seldom employed alone, being given hypodermically in conjunction with morphine and even then only sparingly. The chief indication is the mental excitement, restlessness of acute mania or delirium tremens. Some caution is required in its employment. It should not be used in those "whom nature has made weak," but only in the physically robust. The drug quietens the patient and induces sleep. Its action is that of a cerebral and respiratory depressant, herein lies danger whether the hyoscine be given alone or with morphine.

THE SUMMARY VIEW

The beneficial influence that sleep exercises on the individual and on his recovery from illness manifests itself daily at the bedside, as does the harm consequent upon the lack of it. Idiopathic insomnia is seldom seen—most cases are secondary and symptomatic, having some one or other underlying cause which, when removed, renders sleep possible. Persistent loss of sleep, however caused, may exhaust and delay or prevent recovery; so that treatment must necessarily be symptomatic, and ought to be timely. In procuring enough sleep, strength and vitality are preserved, recovery expedited.

In order to order sleep, sufficient in depth as well as length, will depend not only on the choice of hypnotic and how this is administered, but also upon the thoughtfulness in every detail in the patient's comfort and surroundings. It is generally believed that more than half the success in treating insomnia is to secure for the patient, by sound hypnosis at the start, sleep then following on, even if the effect of the drug given has mostly passed off. A dark, completely silent room is advisable, always possible to obtain in hospital, although obtainable in private practice. A side-ward or a cubicle should be selected, or an end bed in a general ward well off, in order to spin out and prolong any good effect of the hypnotic given. The ears should be lightly plugged with cotton-wool.

Whichever drug is employed should be used with heed to future days and nights. The lax use of any will bring its own defeat, with vexation to the patient and others. In sickness, the dorsal decubitus, low pressure pulse, widening pupils, muttering delirium, inability from loss of muscular and nervous strength to move spontaneously from side to side—these signs may point to exhaustion from insomnia. In sickness become serious which, if not righted, darkens the outlook and forewarns of a failed recovery. With these signs of want of sleep in disease, the patient can no longer think connectedly or take interest in anything. Strange it may seem, but these signs are in great part identical with those resulting from chronic barbiturate poisoning, from which a sharp distinction must be drawn by thorough physical examination, if confusion and the vicious circle snare are to be avoided, or both prolonged insomnia and slow poisoning from a barbiturate may entail a similar profound vital depression. By recognizing the real need for sleep during sickness and securing this expeditiously, such symptoms and signs can be obviated. On the other hand, repeated dosing with "sleeping drugs" is harmful. By giving beyond all need, their noxious effect may seriously jeopardize recovery. When considering the treatment of the sleepless patient, the hurtful part played by the hypnotic in inducing or aggravating delirium and insomnia, has to be kept in mind, this condition, if existing, ought to be corrected and amply so. Perhaps it is wise to restrict the hypnotic drugs employed to the few that are valued, for necessary occasions, this way leads to a better knowledge of their true worth in illness and the avoidance of their confused use. The practitioner will train his judgement to choose the better and reject the worse. The random, crowded giving of various hypnotics only favours faulty and failed treatment, being capable of doing positive harm, seen and unseen, at close or at distant range.

IMPENDING DISSOLUTION

By W N LEAK, M D, B Ch, M R C S

ONE of the penalties paid—or, as some may think, the blessings received—as the result of the increased pace of modern life, is that medical practitioners now seldom stay for long beside the beds of their dying patients. They call in or are called in, do their best, give maybe an injection to ease the passing, speak a word of sympathy or comfort and then are away again to see someone else. Yet there is a real loss to clinical medicine, and perhaps more often suffered, although less often felt, by the consultant than the general practitioner. The fact that the late Lord Dawson of Penn so often had to watch by the deathbed of his illustrious patients, probably helped to make him the acute physician that he was, for such times, to an inquiring mind, are full of unsolved problems and at least teach us how little we really know. We accept the sudden death of angina, coronar thrombosis or cerebral hæmorrhage as inevitable, and seldom ask ourselves if we could have foreseen, even if we could not have prevented, the dramatic event. Sometimes these accidents happen with less suddenness, the time scale is slower—can we intervene with any hope of success? and should we intervene if we can. For it is wise to remember Lord Horder's pregnant saying that "while it is the physician's duty to prolong life, it is not his duty to prolong the act of dying." Where are we to draw the line? Nearly every practitioner must have known cases in which he has perhaps interfered with the act of dying and the patient has unexpectedly lingered on, for months or even years, neither dead nor truly alive, a misery to himself and a burden to those around him. At times it is necessary to do something in order to provide time, if possible, for some relative to arrive, but sometimes—well, it is wiser and kinder to seem busy rather than actually to do anything to delay the inevitable end. Each practitioner must decide for himself according to the circumstances, for as St Paul said long ago "No man dieth unto himself," and when death is imminent the physician has a duty to those whom his patient will soon leave behind.

THE USE OF MORPHINE

In this connexion it may be recalled that at the end of Lord Horder's lecture quoted above he expressed the hope that when his end came he might fall into the hands of a physician who would not hesitate to use morphine, for of all the drugs available to soothe the dying pillow none can compare with it in efficacy when given parenterally. Yet its action is singularly capricious, and it is not usually many years before an inexperienced practitioner gives an injection of morphine to ease, as he thinks, the passage into eternity only to find the next day that the patient is unaccountably better and may even survive for long enough afterwards. In fact, the more freely morphine is used the more difficult it seems to be to prognosticate the end with absolute certainty.

Early in my career I remember a medical missionary of undoubted veracity telling me how when travelling in India he had come across a woman dying in agony from general peritonitis. Operation being utterly impossible he had given her 2 grains of morphine to put her quickly out of her misery. Two years later when he went through the same

illage, a woman, hale and hearty, met him and claimed to be the woman he had so deliberately overdosed

Thirty years' experience has made the story more credible than when first heard, or dying folk are often able to stand relatively huge doses of morphine, although, in my experience, hyoscine is sometimes unexpectedly dangerous, especially in cardiac cases. The beneficial effect of morphine in cases of apparently impending dissolution is both striking and puzzling, but latterly I have begun to connect it with another observation, namely, that it is usually much easier to foretell accurately when death is to take place in hospital practice than when the patient is being nursed at home by his own relatives. Of course the standardized conditions in hospital help, but I imagine that many practitioners must have met cases like the one under my care at this moment.—

The patient is a woman of seventy-nine with both aortic and mitral valvular disease who has had oedema of the legs for years, sometimes gross oedema, but kept moderately comfortable with daily digitalis. A few weeks ago she developed a moderate bronchitis and was looked after by a sister, also with a bad heart but not quite so old or oedematous as the patient. The bronchitis improved but the woman became practically comatose, she lay in bed on her back, took practically no fluids and was obviously at death's door. After being in this state for four days, however, slight signs of improvement took place, consciousness returned in a measure, she took a little fluid, the tongue became cleaner and noisier, the oedema has practically gone and it looks as though the old body may, as they say here, "clog again" for a short while.

What sort of relevance has such a case to the use of morphine? The two may be connected when what has recently been learned about keeping limbs cool when their blood supply is impaired or gangrene threatens is borne in mind. Morphine diminishes metabolism and so decreases the need of the tissues for oxygen. The old woman mentioned, looked after owing to war conditions very inefficiently by her kind but decrepit sister, was but poorly supplied with any artificial heat and must have been much in the condition of a limb kept cool, so the demands of her tissues for oxygen must also have been minimal. Had she been in hospital, carefully nursed and supplied with hot-water bottles, she would certainly have had a better chance of escaping the dire condition into which she fell, but she would also probably have had little chance of getting out of it once she was there, for the demands of her warmed body for oxygen would have overtaxed her exhausted heart and her anticipated demise would have taken place.

WHY DEATH?

Recounting errors of prognosis—and there are others to come—does not perhaps give the reader much confidence in what follows, but the fact must be faced that even in the past the frontiers of death have been by no means so well defined as we have been wont to believe, whilst the many drugs introduced in recent years have placed in our hands powerful instruments for saving the lives of at least some patients whose death would have been certain only a few years ago. It is only necessary to mention penicillin and the sulphonamides in cases of infection to see that this is so, but infections are by no means the only cause of death. When by the bedside of a dying patient the question often obtrudes itself, "Why exactly is this patient dying? What system is at fault, what compensatory mechanism has gone wrong; what function is failing; could anything have been done to avoid it; can anything now be done about it?" Such thoughts turn the occasion into

a sort of examination, which is good for those whose examination days are past, and sometimes stir ideas which may quite legitimately be put to the test of experiment if one is sure they can do the patient no harm and if, as is usually the case, the relatives are anxious for the practitioner to "try anything." My most interesting effort is worth recording, even though I have never been in a position to repeat it. It may, however, serve as an example of clinical thinking and induce some reader to look on these cases as opportunities for hope instead of despair.

In 1938 we operated on a man of sixty-seven, for acute intestinal obstruction following plastic peritonitis from an old perforated appendix. He had a bad chest at the time he developed pneumonia; from which he recovered, only to be followed shortly afterwards by an acute collapse which a consultant diagnosed as a bad pulmonary thrombosis. He rallied from this but a week or so later his condition again worsened, this time slowly; he refused food and later even fluids, gradually sinking into a sort of typhoid state, some picking at the bed clothes, almost constant *subsultus tendinum*, semi-consciousness, rapid and feeble pulse and respiration, with profuse sweating which injections of atropine would not control. The man seemed obviously dying, but what was he dying from? The symptoms did not fit in with any special vascular lesion nor with simple infection. It suggested a deficiency disease, but deficiency of what? He had had abundant supplies of vitamins A, B and D. Pituitrin did not improve him and there was no reason to suspect deficiency of thyroid or pancreas. Apart from the sweating I was familiar with a somewhat similar condition in typhoid and typhus in the last war, and the fact that typhoid is sometimes followed by relative or complete impotence reminded me that I was at the time treating a patient with the fairly recently introduced testoviron, so I decided to see what it might do in the case, at least it could do no harm, and even six hours after the first injection of 10 mgm his condition seemed a bit better, whilst twenty-four hours after there was most marked improvement. He then had a second injection and twenty-four hours after this his *subsultus tendinum* had completely disappeared. After two more injections he was more rational than he had been all through his illness and had, in fact, no recollection of anything from the time of his operation. He eventually made quite a good recovery, although about a month later he developed another attack of pneumonia and died in a few days.

Space does not permit discussion of the various theoretical problems that such a case raises—quite apart from the possibility that it may have been a coincidence in spite of its seeming such a clear case of *propter* and not *post hoc*—but it does illustrate the fact that while there is life there is hope, and that it is worth while for the medical attendant to persevere, not aimlessly doing anything, but cudgelling his brains to see if other bits of knowledge or experience may throw any light on the case in hand, and trying remedies which in less hopeless situations he might not feel justified in doing. A recent case illustrates this well—

An intimate friend, aged fifty-four, in whom I had long anticipated a coronary thrombosis owing to his electrocardiograph and clinical condition, developed pneumonia last January. On February 10 the feared thrombosis took place, very severe and typical, with agonizing pain. Neither morphine subcutaneously nor nicotinic acid intravenously produced any effect and things looked hopeless, so, in order to relieve his pain as rapidly as possible, I eventually gave him $\frac{1}{2}$ grain more morphine intravenously. Within five minutes the pain had gone, the breathing was easier and he sank into a restful sleep to wake up the next day feeling relatively well. On March 4 he had another attack, at least as bad as the first, and death this time seemed even more certain in view of the previous attack. Once again $\frac{1}{2}$ grain of morphine subcutaneously produced no effect, so I gave him another $\frac{1}{2}$ grain intravenously with just as good results as in the first instance. After this his condition deteriorated, with sweats and fever, rising pulse and falling blood pressure. While visiting him on April 6 at night his condition rapidly changed and, although there was no pain, his breathing and pulse failed, the face became cyanosed and then pallid, face and extremities cold, and one could only think some larger thrombosis had occurred. I had given him a dose of morphine almost as soon as I arrived, but with this fresh development I felt justified in giving my friend something to put him out of his misery and I therefore gave him an intravenous dose of hyoscine, morphine and atropine, although it was with great difficulty

I could get into any vein at all. Within a few minutes the whole picture changed, sank on the bed asleep, warmth returned to the hands, colour to the face, and to my surprise next morning he had some breakfast and insisted on doing a cross-word puzzle. Unfortunately, he almost certainly has a malignant endocarditis as well as his coronary with a slowly failing heart and ever increasing oedema.

SIGNIFICANT POINTS

So we come back to our original question. Was I wise in trying to save this man's life at the first, and so prolong the act of dying? Yet when I did think was going to end it I unexpectedly did the opposite and learned afresh the life-saving power of morphine, especially if given intravenously. What *are* the points that make one anticipate a fairly speedy end to a patient? The few suggestions which follow deal mostly with adults, for fortunately experience of death among patients apart from accidents and acute infections, must now be limited, as I find the average age of death in my last completed death certificate book is sixty years and six months—in itself an indication of the increased expectation of life and the need to devote more attention to the ailments and diseases of old people.

Cardiac and respiratory rhythm—It would be possible to go through the various systems of the body—nervous, cardiovascular, integumentary, and so on, and note how their failure prognosticates a fatal end. There is, for example, no mistaking the meaning of a steadily rising pulse rate, whether rising slowly or rapidly. Any steady and progressive deterioration of any bodily function is of ominous significance, even though the patient's condition at the time may seem fairly good. Probably one great advantage of patients in hospital is that, much more commonly than in private practice, temperature, pulse and respiration are charted regularly and a steady rise in any of these is more easily noted. If only they were all charted graphically like the temperature this would be even more obvious to the eye, and earlier notice taken of them when treatment would be more hopeful. Besides these alterations in frequency or intensity there are changes in rhythm to be noted also. The inverted sleep rhythm of post-encephalitics and of some elderly people is of little prognostic significance, but there are alterations of cardiac rhythm which may indicate a more or less speedy end. Modification of any pre-existing rhythm in the course of an illness is probably more important than the actual modification itself, for unless it is accompanied by clear evidence of improvement it almost certainly indicates some new effort of a failing myocardium to adjust itself to increasing demands. The serious prognosis attaching to pulsus alternans is well known, but it is not equally well known that the condition can be recognized by auscultation of the pulse at the elbow in conjunction with a sphygmomanometer. By this means a variation in the strength of the beats of as little as one millimetre of mercury can easily be detected, and if this occurs on alternate beats, pulsus alternans is already developing. It is less easy to speak of alterations in the respiratory rhythm, especially Cheyne-Stokes' respiration. This is usually held to show some alterations in the respiratory centre, but with old people, especially old men, it may be present in sleep for many years before death. It is also often observed after an injection of morphine without being of any serious import. When, however, it occurs in the course of a chronic illness, it has definite prognostic value, and patients do not usually last more than two or three weeks after it is first

noted It is especially valuable as a sign in cases of cerebral hæmorrhage, when it is often exceedingly difficult otherwise to judge whether the patient is to linger for years or to die fairly rapidly

Diminished secretion of urine is a bad sign, often difficult to assess in private practice unless expert nursing is available The statement of friends that a patient is not passing much water is, however, one which should never be disregarded and should cause one to reassess the case lest some danger signal is being missed An earlier danger sign in ambulatory patients is when a person begins to secrete little urine during the day and pass more at night when the strain on the heart is less However, when everything has been said about these more definite clinical measurements, blood pressures, blood sugars and blood ureas, valuable and times indispensable as they all are, I believe that most practitioners sense the approach of death by other means It may be a therapeutic one—the dose of digitalis or what not that kept the patient reasonably comfortable no longer does increasing the dose does not help, the diseased organ is clearly no longer responding as it should or as it used to do, some vital function is becoming hopelessly impaired and the end draws near There is no need to give up at once Mercurial diuresis may succeed when salines fail, or they may help a failing heart to carry on for months or years, or injections of a drug may act when it fails if given orally But for all that, the patient's days are numbered How large the number will often depends upon the skill and mental agility of the practitioner and his power of keeping and imparting hope It may also largely depend upon his willingness to treat his patient as a human being instead of a medical case There are patients who will not live longer if allowed to please themselves towards the end unless there is some urgent biological need for a strict regime, e.g., impending diabetic coma If Lord Horder wishes at his latter end to fall into the hands of a physician who will not be afraid to use morphine, I hope that before I reach that stage I may be allowed the pleasure of pleasing myself in what I eat or drink and how I pass my time What the practitioner often fears may be a short life if a gay one, often turns out to be much longer and happier than he anticipated Towards the end the golden rule should be to do nothing and prohibit nothing unless it is absolutely necessary, or unless the patient demands it or circumstances require it

Other changes—More often still, however, it is some more subtle change that warns the practitioner that the time is nearly up If he knows his patient, and particularly if he has become somewhat friendly with him, it may be little things like lapses of attention or altered mental attitude that give the cue, frequently it may be the person's altered attitude to death itself Anxiety for the end to come may presage death itself, but if a person who has been anxious to live or die becomes apathetic about the issue, it is of much greater prognostic significance A change of position in the bed may be significant, and particularly if a patient persists in lying on his back it is of ill omen, quite apart from any danger of hypostatic pneumonia in spite of the case mentioned earlier Of all the signs the one I dislike most is the development of a *dry tongue* This may, of course, be due at times to breathing through the mouth, but when the tongue has been moist and then becomes dry I always think seriously of the prognosis I believe that it probably represents

the change of the intracellular fluids, i.e., of what may be called the environment of the vital nucleus rather than simple loss of the intercellular fluid, such as is seen in hæmorrhage or other external loss of fluid, which merely affects the environment of the cells. Just giving extra fluids in these cases will not make the tongue moist, and I look on the remoistening of the tongue as the most generally useful sign when any dangerous corner has been passed.

Lagophthalmia and *lustreless eyes* are other serious signs in a patient, and, in the latest phases, coldness and pinching of the nose and a coldness of the breath, and the nasal breath, are signs that death is very near indeed.

Skin changes—I have several times mentioned hypodermic injections. It will not be long before it is recognized that, as a patient draws near death, the skin undergoes a subtle change which makes penetration of the hypodermic needle much less easy than normal. If the illness has been prolonged this change may become visible to the eye as loss of sheen, and appreciable to the touch as a loss of elasticity and the tendency of folds of skin pinched up to persist longer than normal. When these signs go with a quickening and feebling pulse and shallow or laboured breathing it will hardly need a medical practitioner to tell that the death dew and death agony may come at any moment.

FAILURE TO LIVE

Finally, I would say a word about the most distressing impending dissolution of all, that of a baby that does not breathe. Sir Joseph Barcroft's researches on foetal respiration have shown that, experimentally anyhow, the stimulus to respiration at birth is not oxygen lack but stimuli from the skin and muscles. If this is so, much of the accepted teaching on the subject of asphyxia neonatorum is imperfect. If the infant will not breathe, what is required is not more oxygen, still less more carbon dioxide, but something which will make the brain respond to the cutaneous stimulation. This suggests a rationale for the use of *cardiazol* (*leptazolium*)-*ephedrine* which I have used for many years for this condition. An injection of 0.5 c cm. will usually produce a lustily crying infant within a minute or so if administered intramuscularly. Five years ago, when for about ten minutes I could not get a baby to breathe, I gave it another 0.5 c cm. intracardially with an almost instantaneous response, and last year I did the same with equally satisfactory results. When death seems otherwise inevitable such heroic measures are justifiable, and both infants have done well since. *Cardiazol* is a well-known convulsant, which is probably its main action in asphyxia neonatorum, and, although the doses given are quite safe for a baby that does not breathe, smaller doses should be used when breathing has been established feebly, or convulsions may actually occur.

Anyone who like myself has experienced the sorrow a still-birth can bring into a home will excuse in an article devoted mainly to the end of life a reference to failure to live at all, especially as it exemplifies what I feel should always be our outlook on impending dissolution—that nature has wonderful powers of recuperation and response, some of which we can evoke by drugs, some by the way we order the patient's life, some by the exercise of our own personality and faith, and many about which we know nothing at all but for which we should constantly be on the watch.

EYE DISEASES IN THE EAST

By J MINTON, F R C S, Major R A M C

Ophthalmic Surgeon to the Hampstead General Hospital, and Queen Elizabeth Hospital for Children, Assistant Ophthalmic Surgeon to the West End Hospital for Nervous Diseases, London

THE war in the Middle and Far East has brought many into lands where they encounter diseases unknown in Britain. I acted as ophthalmologist to the Baghdad Military Area in 1941 and 1942, and later as ophthalmologist in Ceylon.

The study of eye diseases amongst the natives in Iraq, India and Ceylon gives a complete picture of eye diseases in the Middle and Far East. The diseases occurring in Iraq are typical of any Arab country, and those seen in India and Ceylon are also common farther east in Burma, Malaya, and China. Most medical officers are looking after native troops and native workers. British and American troops stationed in the East are also liable to local infections of the eyes. It is hoped therefore that these notes will be of help to medical officers in the East.

The Middle East (Egypt, Palestine, and Iraq) has been well known from time immemorial for its high incidence of eye infections, and blindness often results therefrom.

EPIDEMICS OF CONJUNCTIVITIS

Every year, in the spring and late autumn, epidemics of conjunctivitis attack thousands of infants and children in each of the above-mentioned countries. The hospitals are crowded with natives who bring their children to the city. In Jerusalem, I saw hundreds of mothers with their children sitting or lying in the courtyard of St John's Ophthalmic Hospital. They make their home in the open courtyard for days, and often for weeks, while their children are receiving treatment for their infected eyes. The conjunctivitis is of a highly virulent nature and often extends to the cornea, causing severe corneal ulcers which may perforate and lead to blindness of the infected eye. The organisms causing the conjunctivitis are the Koch-Weeks bacilli, gonococci, diphtheritic bacilli, staphylococci, and many others. It is interesting to note that gonococcal conjunctivitis is common among children without any infection of the urogenital organs. The infection spreads from the eyes of one child to those of the others. Adults also suffer from epidemic conjunctivitis, but not to the same extent nor with the same severity.

The typical appearance of a child suffering from *muco-purulent conjunctivitis* cannot be forgotten. The child suffers from intense photophobia and therefore cannot keep its eyes open. The lids are red, swollen, and often ulcerated. The child is in pain and often resists the medical officer's or nurse's attempts to open its eyes. In such cases lid retractors have to be used to keep the eyes open, so as to ascertain the extent of the corneal ulceration.

The best *treatment* for all types of muco-purulent conjunctivitis is local and general treatment with sulphonamides—sulphapyridine or sulphathiazole should be given by mouth, the dose depending upon the age and the weight of the child. An infant can be given one half of a tablet three-hourly. This should be continued for several days. The local treatment should consist of gentle swabbing of the eye with saline and the instillation of drops of sulphacetamide 30 per cent (albuclid) every three or four hours, or, if these are not available, sulphanilamide or sulphapyridine powder can be used mixed with cod-liver oil and petroleum jelly, and a paste can be prepared in the following proportions —

Sulphapyridine (powder)	20 per cent.
Cod-liver oil	40 per cent.
Petroleum jelly	40 per cent.

This paste is inserted into the eyes every three hours, and the skin of the lids should also be covered with the paste. The results are excellent, most patients being cured within seven days.

Unfortunately, in the East these modern methods of treatment are used but rarely. In Baghdad, where in 1941 and 1942 I had occasion to visit the civil eye hospitals, the old-fashioned treatment of irrigating the eye and painting the lids with silver nitrate is still the routine treatment. The results are often disastrous, the infected cornea perforates, the iris prolapses, and in many cases the eye is destroyed.

A *diphtheritic conjunctivitis* should be suspected if the conjunctiva is covered with a membrane and the skin of the lids shows extensive ulceration. Diphtheritic conjunctivitis may be present without any associated nasopharyngeal infection. A swab for the detection of diphtheria bacilli should be taken. Should the swab be positive, anti-diphtheritic serum must be administered. Atropine (ointment or drops, 1 per cent.) is indicated in all cases of conjunctivitis associated with corneal ulceration.

TRACHOMA

The native population of the Middle East is highly infected with trachoma. Egypt, Iraq and Persia show the highest incidence of trachoma and, although accurate statistics are not available, it is assumed that about 60 per cent. of the native population of these countries have had trachoma at some period of their life. Trachoma is a chronic infective disease which, again, starts in childhood. It is also highly infective to adults. This disease, which is probably due to a virus infection, starts in the deeper tissues of the conjunctiva of the upper lid and spreads gradually to the cornea, causing extensive corneal ulceration with eventual corneal scarring. The disease lasts for years and requires energetic treatment.

Diagnosis —In its acute stages trachoma is easily diagnosed. The upper lid should be everted and the typical appearance of a follicular conjunctivitis with a corneal ulceration at the upper margin of the cornea should arouse suspicion of trachoma. In less severe cases, a chronic conjunctivitis with scarred pale areas on the palpebral conjunctiva will be found. The presence of blood vessels growing into the cornea (pannus) is typical of trachoma. In old cases the lids are scarred

and deformed, causing the lashes to rub against the cornea (trichiasis). Old cases of trachoma with scarred lids are often infected with muco-purulent organisms. Acute and chronic muco-purulent conjunctivitis is therefore common among the natives of the Middle East.

Treatment—Within recent years general and local treatment of trachoma with sulphonamides has proved most successful. The treatment should consist of general administration of sulphonamide (sulphapyridine or sulphathiazole) and the local application of 30 per cent sulphacetamide drops (albicid) t d s. In seven cases the lids should be painted with 30 per cent sulphacetamide solution daily. In addition to this treatment the follicles of the infected lids should be expressed under a local anæsthetic. Such efficient treatment would diminish the incidence of trachoma in the East, and the appalling blindness resulting from it. Unfortunately, as the result of an insufficient number of competent ophthalmologists, this modern treatment is not being followed up, and trachoma, with its horrible scarring of the lids and cornea and eventual blindness, shows no sign of abating.

VITAMIN DEFICIENCY DISEASES

In India and Ceylon the poor often suffer from vitamin A deficiency, in Karachi and Ceylon I saw many children suffering from this disease which also affects the eyes. In the early stages of the disease children and adults complain of difficulty in seeing in the dark (night-blindness). The conjunctiva shows small yellowish areas (Bitôt's spots). The cornea loses its lustre, corneal ulcers appear, and gradually the whole cornea may necrose. The eye may develop a generalized infection (panophthalmitis) and blindness may follow. Intensive treatment with high doses of vitamin A (cod-liver oil, halibut oil, or shark-liver oil) will save the child's eyes if the treatment is started in the early stages of the disease. The children are usually marasmic and generally undernourished and therefore need careful general feeding.

EPIDEMIC PUNCTATE KERATITIS (KERATO-CONJUNCTIVITIS)

Epidemics of conjunctivitis do not occur in India and Ceylon with the same regularity every summer as they do in the Middle East. The mild Koch-Week conjunctivitis is common in the summer. In certain provinces of India (Bombay, Madras and Calcutta), and also in Ceylon, epidemics of infective punctate keratitis (epidemic kerato-conjunctivitis) occur in the summer. This disease attacks adults. It starts with pain in the eyes and photophobia. There is very little discharge from the eyes. In severe cases the glands in front of the ear (pre-auricular glands) may be tender and enlarged. The eyes are red. If a drop of 1 per cent fluorescein solution is instilled into the eyes a number of small stained spots will be seen on the cornea. This disease takes weeks to clear up and often leaves small corneal scars which may disturb the vision. A virus is responsible for these infections. Sulphonamides are not of great help in the treatment of the condition. The patient gets great relief from frequent hot sponging of the eyes (hot spooning), atropine, and

' glasses Mild antiseptic drops, argyrol 10 per cent, or mercurochrome or 2 per cent, are also helpful

INCIDENCE AMONG EUROPEANS

The foregoing description of eye diseases in the East may make some apprehensive of going out to these parts, where the risk of infection to the eyes is so great. There is, however, no need for undue concern, as the incidence of eye infection among Europeans living in the tropics is low. In the nineteenth century, during the wars in the East, epidemics of eye diseases were common among the British and French troops. At that time hundreds of soldiers came back from the East suffering from trachoma. The poor hygienic conditions which then existed among the troops were responsible for the rapid spread of infection. In this war, troops in the East suffer from few epidemic eye infections. Cases of blepharitis, conjunctivitis, with corneal ulceration, and keratitis, will be seen in all hospitals, but in small numbers. Many British nurses are attached to Indian hospitals, nursing Indian soldiers. The latter often suffer from trachomatous infections of the eyes. It is therefore essential that nurses should be aware of the fact that trachoma is infective and that the necessary precautions should be exercised when treatment to the eyes is being carried out. Efficient modern treatment with sulphonamides (general and local treatment) has been of great help in reducing the complications of this disease and accelerating the recovery of these soldiers. Fortunately, cases of trachoma are extremely rare amongst British troops. During the two years I stayed in the East, I never saw a case of trachoma in a British soldier.

EFFECTS OF THE TROPICAL SUN

The tropical sun and the cloudless sky of the Middle East and India have a high content of ultra-violet radiation. This sometimes causes a mild conjunctivitis in people who are exposed to the sun for many hours. The tropical helmet and peaked cap provide a certain amount of protection but it is advisable that drivers and others who work in the open should wear dark glasses. The glare reflected from the sand of the desert and the water of the seas and rivers causes screwing-up of the eyes, with resultant eyestrain and headache. Some people are highly sensitive to the glare of the tropical sun. Dark sun-glasses would prevent all these symptoms. Many people are under the impression that the tropical sun is harmful to the eyes and is responsible for eye diseases, this is quite untrue.

CHILD HEALTH

XV—THE BLIND CHILD

By R RAMSAY GARDEN, M.B., CH.B., D.P.H., D.O.M.S.

*Surgeon, Bristol Eye Hospital, Ophthalmologist to Bristol Corporation Medical Services
and to the Royal School for the Blind, Westbury-on-Trym, Bristol*

IN the course of the last quarter of a century, there has been a steady decrease in the number of those whose blindness dates from infancy, and the proportion of the total blind population in this category showed a fall of nearly 50 per cent from 1919 to 1943. This is an encouraging state of affairs, resulting largely from the success of ante- and post-natal prophylaxis, of notification and, more recently, of improved chemotherapy in reducing the risks and effects of ophthalmic neonatorum, formerly responsible for so many of the cases admitted to schools for the blind. Blindness due to this eye disease has been comparatively rare in recent years and, although renewed vigilance is essential under war-time conditions, the prospects of practically eliminating this as a cause are favourable. Nevertheless, there remains still a considerable group whose sight is so seriously impaired by congenital, developmental and other defects arising in childhood that they have to be educated and taught the art of living by special methods. Medical practitioners are at times consulted about the management of these children, and the object of this article is to give those not familiar with the care of the blind child some information with which they can encourage the distressed parents, to indicate the difficulties which may arise, and to arouse interest in cooperating with the voluntary and official organizations which deal with the problem.

HISTORY OF EDUCATION OF THE BLIND

Blindness, especially in the young, is of all physical afflictions the one which probably evokes most sympathy, and happily in the course of several generations there has been evolved a system of education and after-care which mitigates the misfortune and handicap to an extent perhaps not fully realized by the majority of people. Although concern for the welfare of blind people has its origin several centuries in the past, when various religious foundations and philanthropic individuals worked to alleviate the sufferings and poverty of those deprived of sight, it was not until 1784 that any organized system of education for blind children was established. Here France led the way, the first national school for the blind in Europe—the “Institut National des Jeunes Aveugles”—having been founded in that year by Valentin Haüy, in Paris. In 1791, Liverpool opened the first institution of the kind in this country, followed soon after by Bristol, whose School of Industry for the Blind started in 1793, by Edinburgh in the same year and by London with a school in Southwark in 1799. Haüy was also the first to emboss paper with raised characters to provide reading matter for the blind, and to institute printing in relief, whilst Braille, a pupil and later instructor at the school founded by Haüy, developed and published in 1829 the six-point system which bears his name, and which is now used throughout the world for blind education of all kinds—literary, musical and scientific. Since these pioneer schools were opened, similar institutions have been founded all over this country and in most civilized foreign lands.

In Great Britain, the majority of schools for the blind are managed by voluntary associations, but the Education Authorities make the fullest use of their organization and in return accept financial responsibility for maintaining most of the pupils. This also applies to higher education, secondary and technical, and to the workshop training of those leaving school.

THE BLIND INFANT

Home training—Although the education of blind children under the age of five years is not compulsory, local Education Authorities have power to provide it from the age of two years. As explained later, it may be advisable in some cases for the child's early training to be carried out in a nursery school, but there is little, if any, doubt that the best place for an otherwise normal blind child under school age is at home, provided the conditions are good and the parents are able to cope with the situation. In the case of a blind baby, once the advice of an ophthalmologist has been obtained as to the possibility of remedial treatment, every effort should be made by the parents or those in charge of the child to teach self-reliance. The mind receives the preponderance of its impressions of the outside world through the sense of sight, and other faculties must be called upon and developed to help overcome the visual deficiency. Over-protection, pampering and taking the line of least resistance, must especially be avoided in the upbringing of a blind infant. If not encouraged to move about and take an interest in what is going on, the child will sit still in one place or at most grope about timorously when obliged to change position, the physique will deteriorate and the mentality stagnate. The child should have as much as possible of the company of an older sighted person, and frequent opportunities of playing out-of-doors among normal children, reasonable precautions being taken for safety. The blind infant should be taught to walk at the usual age, to go up and downstairs, to wash, dress, undress and feed itself, and to recognize all manner of objects and materials by their shape and texture. Disagreeable habits and grimaces must be checked, ungainly postures and attitudes corrected, and every care taken to ensure that the child's behaviour is reasonably good. A sensible parent can accomplish all this, but may need encouragement and guidance from the family practitioner and the staff of the local blind organization, who will always give sympathetic assistance. The training of a young blind child requires much patience, tact and understanding, but a good parent can make a real success of it. Then when the time comes for going to a blind school, the child can enter with confidence into the life there, unhindered by the need for learning the elementary rules of behaviour which are ordinarily acquired in the home.

Nursery school training—In the case of a blind infant whose parents are poor, ignorant, ill-housed or over-burdened with other domestic worries, the most satisfactory solution is for the child to be admitted to one of the Sunshine Homes, maintained by the National Institute for the Blind. Two of these are for normal blind, and one for retarded blind infants. In these excellently equipped residential schools, provision is made for the training of blind babies from birth to school age, and the following extract from the Institute's Annual Report for 1937-8 well describes the upbringing and education which is provided—

The educational methods adopted at the Homes aim to stimulate the desire for independence, self-reliance and thoughtfulness for others, by free movement in the house and

grounds and excursions outside, instruction in personal cleanliness, dressing, undressing, tidying, caring for dolls and toys, the care of animal pets and flowers, physical exercises and games. The children are mentally equipped, as they grow older, by speech training, instruction in the elements of Braille reading and writing, simple Scripture talks and rhymes, nursery songs, appreciation of music, handwork, and the development of the sense of numbers. Their free natural life in the atmosphere of serene, cheerful activity is ideal and as a result you get vigorous little minds in vigorous little bodies. Only the eyes are blind, behind them is the perceiving brain, which, with agile fingers, nimble legs and alert little noses to aid it, is day by day acquiring habit, forming personality and developing imagination. The present-day Sunshine children are very different from the blind infants of other days who knew nothing of the outside world and were apparently content to stay within four walls, listen to a gramophone and walk round the garden in tails, or behind the other. The elder children are at home in town, they know the shops by the smell of the goods, they "sense" spaces, gateways, archways, walls, by the echo of the footsteps.

SCHOOLS FOR THE BLIND

Once school age is reached, the blind child's education is carried on in one of the schools provided by voluntary organizations or by the Ministry of Education. As is usual with any advances in social welfare in this country, the urge to act arose in individuals and groups of people, who, seeing the need for improved conditions, voluntarily found ways and means to bring them about. So in the education of the blind, the activities of the voluntary associations led gradually to action by the State. A Royal Commission in 1889 issued a report based on the experience of voluntary blind institutions, and their recommendations were embodied in the Elementary Education (Blind and Deaf Children) Act 1893, by which all school authorities were obliged to provide education for blind and deaf children resident in their area at schools certified for the purpose by the Board of Education. Subsequent legislation provided for further training of the same types of exceptional children, after the age of sixteen, in technical and other subjects. The latest regulations, issued in connexion with the recent new Education Act, make it compulsory for "pupils who have no sight or whose sight is or is likely to become so defective that they require education by methods not involving the use of sight" to be educated in a special school, and thus shall be boarding school, although there will be no objection to the admission of blind pupils, whose homes are in the vicinity of a boarding school, as day pupils. Hitherto there have been a number of day schools for the blind, but the advantages of educating children thus handicapped in residential schools are obvious to those experienced in the care of the blind. Apart from difficulties arising from the fact that the children often live at long distances from the nearest blind school, it is easier to secure efficient organization and continuous education in an institution sufficiently large to provide classes for all ages of blind children, i.e., in the usual special school age-group, from five to sixteen years. Furthermore, it is better for their physical welfare that they should be grouped in residential schools where adequate medical, ophthalmological and dental supervision can be readily obtained in addition to opportunities for the physical training, remedial exercises and games suitable for the blind. Generally speaking, thanks to the use of special methods, e.g., Braille for reading, writing, mathematics and music, and relief maps for geography, blind children can obtain an elementary education which compares favourably with that acquired by the sighted. Often the need to memorize so much of the work and to rely upon oral methods may actually give the blind some

advantages when it comes to expressing themselves. The manual work taught includes bead-threading, modelling, raffia-work and other elementary handicrafts for the younger pupils, basket work, rug-weaving, woodwork, mat-making and for the older ones, with domestic science, sewing and knitting for the girls. Music and singing occupy an important part in the curriculum, and these subjects with weaving, piano-tuning, typewriting and Braille shorthand may be developed in the later years at school if the pupil shows an aptitude in one or more of them sufficient to make further training justifiable.

Secondary education is provided for blind boys at Worcester College and for blind girls at Chorley Wood. These colleges prepare their pupils for the usual School Certificate and other examinations, and have an excellent record of successes in the latter and at the Universities. The Royal Normal College admits pupils from the age of five to twenty-one, giving special attention to the teaching of music, pianoforte tuning, stenography and typewriting, in addition to providing a sound general education. For most of the blind children who do not go to secondary schools, courses of training in some form of manual work are provided at the workshops recognized by the Ministry of Education.

The administration and maintenance of the Sunshine Homes, the two secondary schools for the blind, a school for mentally retarded blind children, a massage school, and a clinic and institute of massage and physiotherapy are activities of the National Institute for the Blind, which are probably not so widely known amongst the public as its great publishing department, which prints embossed literature of all kinds (including textbooks and scientific treatises for students) for blind persons of all ages. For further details of the vast amount of work being done for the blind, those interested are referred to the reports issued from time to time by the Institute and by the numerous voluntary organizations throughout the country. Fuller information about schools, workshops and physical training for the blind is to be found in several of the Annual Reports by the Chief Medical Officer of the Board of Education, and other official publications.

THE PARTIALLY SIGHTED CHILD

In a number of blind schools, classes for the partially sighted have been established, and certain advantages have resulted from this arrangement. In the school with which I am associated, all the pupils get practice in using Braille up to the age of eleven, and the partially sighted can, if necessary, be taught by this method should the condition of the sight require it at any later age. Again, if it is desirable that the sight of a myope, for instance, should be rested for a period, it is easy to arrange for education to be carried on by oral methods, with or without Braille. On the other hand, it is desirable to let the educationally blind make use of any sight they may have (and some have a considerable amount), so long as no harm is likely to be caused to the eyes. To those and to the few whose sight shows sufficient improvement while at school, partially sighted methods in part or as a whole are readily available. Blind children benefit by contact with those having better sight, who inevitably convey their own impressions and descriptions of things seen to their less fortunate companions. In sports, games, country dancing and dramatics, an occasional warning or touch on the arm from those with sight will suffice to keep the blind performer right in carrying out the various evolutions.

and movements with success. For the partially sighted, this habit of being helpful to their blind companions forms an important part of character training, almost unconsciously acquired.

MEDICAL SUPERVISION

In what has been said so far, the emphasis has been mostly on early training and education, but a few observations on some special medical aspects of the question may be helpful. The requirements are in the main those associated with any residential institution for the young—regular medical and dental inspection, Schick testing and immunization, the control of infective disease—but a fair number of entrants to blind schools require treatment for defective physique and nutrition. As the blind tend, for example, to develop round shoulders and other deformities, special attention is given to posture, and remedial exercises as well as routine physical training may be required.

Physical training—Whilst on the subject of physical training, it may be mentioned that blind children can engage in many of the sports and games which form part of a normal school life. It is true that ball games have to be modified, but most free-standing and gymnastic exercises are suitable, whilst country dancing, swimming and, for older pupils, rowing with a sighted cox can be carried on with success. In the sports field, the high and broad jump, obstacle races and running with wire guides are all possible as athletic exercises for the blind. The improvement in physique and health which takes place in many of the children as a result of suitable diet and exercise is often remarkable.

Ophthalmic care—Whilst it would be out of place in this article to enter into ophthalmological details, one or two points may be usefully mentioned. So far as possible, any surgical and optical treatment required by the blind child should be completed before entry into the school. Medical treatment, e.g., anti-specific therapy, can be carried on while the child is still receiving education. A completed copy of the official form of blind certificate and the latest prescription for glasses, if worn, should be sent with the admission papers, as well as any information about the eye condition and its previous treatment, family history of blindness, and such-like, which might be helpful to the ophthalmic surgeon attached to the school. On admission, full clinical details of the eyes and sight are entered on a special record card, and the examination is repeated at least once, and usually twice, a year throughout school life. In addition, many of those who have left school are kept under periodical observation afterwards until the ophthalmological condition has become stabilized. It should be added that all decisions as to the type of education suitable for each child on entry and throughout school life are made by the ophthalmologist, who also advises as to the suitability of occupations favoured by the partially sighted when they approach the school-leaving age.

CONCLUSION

Any reluctance on the part of parents to send their child to a school for the blind is usually overcome once they have paid a visit to the school. Blind children generally form a happy, cheerful community, and are given every opportunity to grow up as useful, self-reliant citizens. Some indeed, although born blind, have come to occupy notable positions in life, and to all there is a life-long assurance that their interests and security are matters of importance, both to the State and to the many organizations, great and small, which work so devotedly on their behalf.

NOTES AND QUERIES

SEBORRHOEIC DERMATOSES IN
WAR TIME

QUESTION (from a subscriber in Herts)—I should be glad to know if there has been an increase in seborrhoeic dermatoses of the anal, perineal and axillary regions during the war and, if so, what are the probable causes. I have been impressed by the number of people in all walks of life who appear to be suffering in this way and by the intractability to treatment. There is much itching at night, the eruption is typically seborrhoeic, and threadworm infestation has been ruled out. I would appreciate guidance as to treatment.

REPLY—There has been a notable increase in the seborrhoeic dermatoses of all types during the war and this increase is ascribed to the anxiety connected with war, the relative excess of starch, and the probable lack of vitamin B complex in the diet. It is obvious that in the minor neuroses the sweat and sebaceous glands are more active and therefore the folds of the skin are macerated and susceptible to the usual skin organisms. Treatment consists of good psychological management of the patient, restriction of starchy goods, extra vitamin B complex in the form of bemax and yeast, raw fruit and vegetables, and appropriate sedatives to control the irritability. The addition of tincture of belladonna, 7 to 10 minims, to an alkaline bromide mixture is of great value, unless the subject is predisposed to boils. Phenobarbitone, $\frac{1}{2}$ a grain once or twice a day, p.c., is also useful. Lotions and powders are the most suitable applications for the flexural lesions in which greases retain sweat and encourage infection. A useful lotion is phenol, 10 minims, industrial methylated spirit, 120 minims, solution of mercuric chloride or solution of lead to 1 ounce. 3 per cent silver nitrate in distilled water may be valuable or 2 per cent. of phenol and sulphur in calamine lotion. Fissan ichthyol powder is a pleasant and suitable application.

REGINALD T. BRAIN, M.D., F.R.C.P.

MENOPAUSAL SYMPTOMS AFTER
PANHYSTERECTOMY

QUESTION—A woman aged fifty underwent a panhysterectomy four years ago for uterine fibroids, and it appears that no ovarian tissue was left behind. Since then the patient has had periodic outbursts of temper and has complained of nervousness, hot flushes and throbbing headaches. Would you kindly suggest a suitable form of treatment for this patient?

REPLY—After removal of the ovaries and, indeed, even in cases when the menopause comes on naturally, occasionally there are severe mental disturbances and alteration in a patient's mental

make-up, and especially increased irritability. These symptoms frequently respond to small doses of oestrogenic hormone, and in this particular case I would suggest giving her $\frac{1}{2}$ mgm stilboestrol twice daily for some weeks, together with a bromide mixture. Some proprietary firms produce a tablet containing stilboestrol and bromide, and these are particularly useful.

DOUGLAS MACLEOD, M.S., F.R.C.P.,
F.R.C.S., F.R.C.O.G.

EARLY SYMPTOMS OF RAYNAUD'S
DISEASE

QUESTION (from a subscriber in India)—A woman patient of mine, age forty-nine, barren, has had chilblains on her toes for the last twenty years, but for the last five years she has had, in addition, absolutely bloodless white fingers in winter whenever her hands come into contact with water or even wind. Colour returns when the hands are put in hot water or when they are warmed. Treatment of various kinds is of no avail. Would this condition lead to Raynaud's disease and, if so, what measures should be adopted to prevent it?

REPLY—Clearly this patient is exhibiting Raynaud's phenomenon, and possibly she has Raynaud's disease. The onset is rather late in life for the latter, her symptoms having started at forty-four years of age. The point can be settled only by determining if any organic disease of the vessels is present, e.g. thromboangiitis obliterans, syphilis, premature arteriosclerosis, or late sclerodactyly. Furthermore, it would be wise to exclude cervical rib, although I do not believe it is ever responsible for such symptoms unaccompanied by others of more suggestive nature. The probability is that this is Raynaud's disease. The general measures of clothing the body to the extent of discomfort, and the avoidance of provocatives are too well known to need description. I strongly recommend the use of carbachol by ionization as the best specific treatment. The aim is to induce dilatation of the digital arteries. This can be achieved by the daily application of 0.2 per cent solution by a pad placed at the base of the fingers. A 30 milliamp current is used for fifteen minutes. After a fortnight the treatment can be reduced from daily to bi-weekly applications. Systemic effects of carbachol may be produced. Sweating, faintness and abdominal griping are the common ones. Reduction of the strength of the solution may be all that is required to prevent them. If this step interferes with the local result, then the original strength should be used, but the patient should be given from 10 to 15 minims of tincture of belladonna half an hour before each session.

A. H. DOUTHWAITE, M.D., F.R.C.P.

PRACTICAL NOTES

TESTOSTERONE PROPIONATE IN THE PREVENTION OF RECURRENT POST-OPERATIVE MAMMARY CANCER

A NUMBER of patients with mammary cancer, who had undergone mastectomy, have been treated by weekly injections of testosterone propionate as a prophylactic against post-operative recurrences, and the results, which show an improvement rate of about 100 per cent, are recorded by A. Prudente (*Surgery, Gynecology and Obstetrics*, June 1945, 80, 575). In a table giving the results with and without testosterone propionate during a post-operative period of more than three years, the survival rate without recurrences in eight patients grades I and II and thirteen patients grade III was 100 per cent, of three patients grade IV, one survived without recurrence. All these patients received testosterone propionate. In patients not receiving testosterone propionate the rate for survival without recurrence was 100 per cent in grade I, in grade II, 71.4 per cent, in grade III, 30.7 per cent., and in grade IV nil. In another table showing the results of treated and non-treated patients with and without axillary metastases, the survival rate without recurrence in the testosterone-treated patients without metastases was 100 per cent, and in those with axillary metastases 87.5 per cent., in the patients not receiving testosterone propionate the survival rate without recurrences in those without axillary metastases was 100 per cent, and in those with axillary metastases 36.8 per cent. The dosage used and recommended by the author is an initial dose of 25 mgm. weekly rising to a maximum of 175 mgm. weekly, the establishment of the required dosage depending upon the development of the individual case and the reactions of the patient. Patients with diffuse carcinoma (grade IV) should receive a dose of 175 mgm. weekly, despite any secondary amenorrhoea or signs of virilization, this dosage should be maintained for one year, then reduced to 100 mgm. weekly for the second year, 75 mgm. weekly for the third and fourth years, and 50 mgm. weekly for the fifth year and thereafter. Treatment should be continued indefinitely. In carcinoma solidum (grade III) the average weekly dose should be 75 to 100 mgm. for the first year, depending upon the presence or not of axillary metastases, dosage can be decreased or even interrupted if signs of virilization or prolonged amenorrhoea occur in younger patients, and as time proceeds the dose can be lowered, but a minimum dose of 25 mgm. should be continued with as maintenance. In carcinoma adenomatousum (grade II) the dosage depends upon the

presence of axillary metastases, if present dose should be 75 mgm. weekly, if not so weekly for the first year. In young women dosage can be adjusted according to symptoms. In cases of adenoma (grade I) a weekly dose of 25 mgm. is sufficient and need not be prolonged beyond one year. In addition to the secondary reaction of virilization, which occurs almost exclusively in women, and of disturbances of menstruation including amenorrhoea, early cessation of menstruation frequently occurs in patients in the ages of forty and fifty.

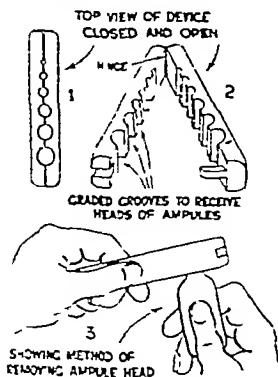
A POCKET MICROSCOPE

A "NEW compact microscope" is described by D. J. O'Brien (*New England Journal of Medicine*, April 26, 1945, 232, 475). It weighs 1 lb. and its dimensions are $4\frac{1}{2}$ inches $2\frac{1}{2}$ inches wide and $5\frac{1}{2}$ inches in height. Reduction in size has been attained by bending the light rays through four right-angle prisms and it is claimed that the refractory light inevitable to such a system is no more than the similar loss of light in binocular microscopes. Ordinary eyepieces and objectives (low-power and oil immersion) can be used. A focal length of 175 mm. is maintained. Sub-stage condensing of light is accomplished by using a mirror of short focal length, and function of a diaphragm is performed by mirror adjustment worked by a small knob on the side of the base. The microscope is provided with both a coarse and fine adjustment.

THE BLOOD PRESSURE IN CHILDREN. HITHERTO the data upon which has been based the normal blood pressure in children has been relatively scanty. A preliminary report has now been published of the findings of a large-scale investigation, based upon determinations of the blood pressure made by one observer in 3,580 school children, who have been under observation from the ages of six to sixteen years (A. W. Graham, E. A. Hines and R. P. Gage, *American Journal of Diseases of Children*, April 1945, 69, 203). The systolic blood pressure ranged from 92 mm. Hg. at the age of five years to 122 mm. Hg. at the age of sixteen, the corresponding figures for diastolic pressure being 52 and 62 mm. Hg. There was a linear increase of both systolic and diastolic pressures with each year of age, no appreciable sex difference was noted, and no apparent increase in variability of blood pressure occurred with increasing age and this was most marked during puberty and adolescence, particularly in girls aged ten to thirteen years.

MECHANICAL DEVICE FOR OPENING AMPOULES

A MECHANICAL device to facilitate the opening of biochemical ampoules is described by F. J. M. (Medical Journal of Australia, April 28, 1945, 32, 429). The device, which opens like a nut-cracker, comprises a graded series of cylindrical receptacles. After circumferential filing with a good file, the head of the ampoule is placed in the particular receptacle, which twists it without free play, and the body of the ampoule, which is gripped with the right hand, is gently snapped off. The heads of ampoules made of firm non-resistant glass, which frequently prove refractory to filing, can be removed with ease in this manner.



ampoules ranging from one-fifth to one-half three-quarters of an inch, in a series of five or six, meet all requirements, including the large penicillin ampoule of 20 c.cm., which has a head half an inch in diameter. The device is the work of a semi-invalid wood worker, and inquiries should be addressed to the author, c/o The Medical Journal of Australia, The Printing House, Seamer Street, Glebe, Sydney, N S W.

"THE NEW ULCER"

A NEW type of ulcer, termed "the new ulcer of Port-Said," its etiology, pathology and treatment, is described by A. H. Hafez (Journal of the Royal Egyptian Medical Association, November 1944, 27, 473). The ulcer, which has a seasonal distribution, being most common in the period between November and March, is more prevalent among the poor and underfed, thus indicating an etiology of malnutrition and deficiency diseases. It starts as a small pimple, or as the result of slight trauma, most commonly on the external side of the leg, which forms a vesicle that erupts and develops into an ulcer, usually oval or circular in shape, with shelving edges and the floor covered with septic greyish slough. The base of the ulcer is supple and not attached to the underlying tissues, and the surrounding skin is usually of normal colour but

may be darkish red and brawny. Characteristic features of the ulcer are (1) it is usually single, rarely multiple, (2) it resists and spreads in spite of ordinary treatment with antiseptic dressings or oxidizing agents, (3) it has been met with more frequently during the war. Smears taken from many of the ulcers showed by simple staining a mixed flora of staphylococci, streptococci, micrococci and short bacilli. Patients with this type of ulcer were told to take good quantities of garden rocket (*eruca sativa*) lettuce, radish and clover, and the diet was supplemented by injections of vitamins B and C, twice weekly. The ulcers were dressed with cod-liver oil. The result is stated to have been "marvellous"—the ulcers became stationary for a time, sloughing disappeared from the floor of the ulcers, followed by healthy red granulation and final healing in a short time (not exceeding three months), leaving a thin, supple, white scar.

CHEMOTHERAPY IN TUBERCULOSIS

A CRITICAL evaluation of the present status of chemotherapy in tuberculosis is provided by H. C. Hinshaw, W. H. Feldman, and K. H. Pfuetze (Annals of Internal Medicine, May 1945, 22, 696). Three sulphone derivatives have been found to be active against tuberculous infection in the guinea-pig: promin, diasone, and promizole. In this animal the results of treatment with these drugs may be summarized as follows—(1) the life of animals that continue to receive treatment can be prolonged indefinitely; (2) macroscopic tuberculous lesions diminish in size or disappear following such treatment; (3) histologic evidence of healing has been obtained in the form of fibrosis, encapsulation or even calcification. In man, however, the results have been no more than encouraging. In the case of promin, it has been found that only one-third to one-half of the patients can tolerate the dosage required to maintain an adequate concentration of the drug in the blood stream, and even when full doses can be tolerated, the results have only been "encouraging but by no means convincing" or "cautiously optimistic." Diasone has not been in use so long as promin and, whilst some observers give encouraging results, others are more reticent and prefer to await fuller observations. Promizole is claimed to be of low toxicity for man, but its therapeutic value has not been confirmed, although promising results have been obtained in the treatment of non-pulmonary tuberculosis, such as cutaneous tuberculosis, tuberculous lymphadenitis and tuberculous sinus. It is thus evident that none of these sulphone derivatives has a dramatic effect upon the tubercle bacillus comparable to that of the sulphonamides or penicillin upon pyogenic organisms, and, whilst full and carefully controlled clinical trials are clearly indicated, it is essential for practitioners to insist meanwhile

upon their patients submitting themselves to the well-tried forms of treatment, such as sanatorium regime and collapse therapy, until definite conclusions can be drawn as to the efficacy of these new chemotherapeutic agents

INTRAPERITONEAL INJECTIONS OF NOVOCAIN FOR GASTRIC ULCER PAIN

AN account of the results obtained by C. Auguste and M. Héraud (*L'Echo médical du Nord*, 1944, 15, 545) by means of intraperitoneal injections of novocain in cases of refractory gastric or duodenal ulcer pain is given by L. Roques (*Presse Médicale*, July 14, 1945, 53, 388). After ascertaining that there is no hypertrophy of the liver or risk of its being injured, the injection is given in the median line at equal distance from the umbilicus and the xiphoid, or, if the patient has undergone laparotomy, at the right or left of the scar, according to the site of the pain. The patient, who should be fasting, lies in the decubitus dorsal position with the buttocks raised on a cushion. A short bevelled needle, 1 mm in diameter and 6-7 cm long, is plunged through the abdominal wall into the peritoneal cavity, the patient being told to avoid deep respiratory movements. After seeing that there is no aspirated blood in the syringe, a warmed 5 per cent aqueous novocain solution is injected in dosage of 7-8 mgm novocain per kgm body weight; this dosage is never exceeded. Of thirty-eight patients treated, nineteen obtained complete or considerable relief, in nine there was only slight improvement, and in ten no modification of the pain. The relief from pain occurs at the latest one to two hours after the injection and lasts three or four days, or even longer. In some cases there was no recurrence of pain, in some in which there was a recurrence the pain was not so intense as primarily. Some patients were effectively relieved after three to four injections. The treatment, which is purely symptomatic and in no way should take the place of medical or surgical measures, is indicated when ulcer pain persists in spite of usual treatment; it can also be used to calm patients before operation. The only contraindication would seem to be a threat of perforation.

THE TOXICITY OF BORACIC ACID OINTMENT

WHILST there is no reliable evidence that boracic acid can be absorbed through the intact skin, evidence is accumulating that the use of boracic acid, either as an ointment or in solution, in the treatment of extensive burns, wounds or granulation tissue, or as an irrigating solution, is not without danger. The latest investigation of the subject (C. C. Pfeiffer, L. F. Hallman, and I. Gersh, *Journal of the American Medical Association*, May 26, 1945, 128, 266) confirms previous

findings that boracic acid applied as an ointment or in saturated solution is a cumulative poison, and the investigation suggests that it should no longer be used for this purpose, but should be replaced by other therapeutic agents that are more active and less toxic. In the experimental animal, toxic effects were produced in the brain, spinal cord and the kidneys. There was evidence of any deleterious action upon blood-forming organs, and the liver was slightly affected. Irrigation of cavities with a 5 per cent solution was followed by almost complete absorption of the boracic acid. Pathologic changes were produced in the central nervous system by treatment of a burn involving only 4 per cent of the body surface with the U.S.P. 10 per cent boracic acid ointment. The only effective antidote was found to be the intravenous injection of large amounts of a solution consisting of 50 per cent Ringer's solution and 50 per cent plasma.

SULPHATHIAZOLE OINTMENT FOR THE PREVENTION AND TREATMENT OF INFANTILE PYODERMAS

AN ointment consisting of sulphathiazole 5 per cent, sodium lauryl sulphate 1 per cent, stearic alcohol 10 per cent, cetyl alcohol 3 per cent, spermaceti 10 per cent, glycerin 10 per cent and water 61 per cent has been used by C. Weymuller and Elizabeth J. Ittner (*American Journal of Diseases of Children*, May 1945, 283) as a prophylactic against impetigo and pyoderma for 3,205 new-born infants during a period of two years. The routine adopted was as follows—Immediately after the new-born infant had been cleansed with sterile cornstarch, 15 gm. of the ointment was applied all over, after twelve hours a thorough bath was given. If no pyoderma developed, no further treatment was given, but affected infants were isolated, the lesions opened under 70 per cent alcohol and repeated applications of the ointment made. The nursery in which the affected infants were placed was closed to all new admissions, each infant was again anointed with 15 gm. of the sulphathiazole ointment. The procedure was repeated if fresh outbreaks occurred. The results are reported to have been excellent—from August 1942 to August 1944 only 13 cases of sporadic pyoderma occurred in 34 nurseries, without spread to infants in the same nursery or those in adjacent nurseries. Significant changes were noted by blood examination or urine analysis. Forty-nine of the 3,205 infants who received prophylactic ointment were readmitted for serious illness requiring full dosage of sulphonamides. In forty-three the compound employed was sulphathiazole. There was no instance of sensitization to sulphonamide compounds.

REVIEWS OF BOOKS

Treatment of Acute Intestinal Obstruction

By JUDSON T CHESTERMAN, M.R.C.P.,
F.R.C.S., F.A.C.S. London J & A.
Churchill Ltd., 1945 Pp viii and 116
Illustrations 13 Price 10s 6d

THIS small monograph gives evidence of the wide experience and reading of the author. The art concerned with general considerations is introduced by, and founded on, two chapters on pathology—the first, on the pathology induced by acute intestinal obstruction, the second, an original approach, on the pathology induced by the release of acute intestinal obstruction. In diagnosis, after careful discussion of the clinical features, most stress is laid on X-ray examination—"if the radiograph is taken in conjunction with other findings, it gives help which can be obtained in no other way." Under treatment, particularly valuable are the pages on the difficulties in the use of the Miller-Abbott tube. In the second part of the book a more detailed consideration is given to special points in the management of the main types of intestinal obstruction. This part is full of useful hints and in nearly every chapter even the surgeon experienced in this type of case will find some special point of value, e.g., simple rules for the treatment of obstruction due to developmental errors of the mid-gut, and the tip about the passing of a rectal tube with the patient in the knee-elbow position in volvulus of the pelvic colon. The book is well produced and the references are full. The pleasure in reading it was slightly marred by an occasional misprint and error in punctuation.

Fractures and Orthopaedic Surgery for Nurses and Masseuses

By ARTHUR NAYLOR, Ch.M., M.B., F.R.C.S., F.R.C.S.Ed.
With a foreword by ERNEST FINCH, M.D.,
F.R.C.S. Pp xii and 288 Illustrations 243
Edinburgh E & S Livingstone Ltd., 1945 Price 16s

THIS beautifully produced book for nurses and masseuses fills a clamant need, for, as the author points out, almost one-fifth of their surgical work is in orthopaedics and the bare minimum of instruction is given in their course. It is written with the object of showing the nurse how the principles of general surgery are applied to the orthopaedic specialty, and as a supplement to the surgical lectures. Of the three essentials of treatment—prevention of deformity, correction of deformity, and maintenance of correction—the greatest is prevention, and the author impresses this on his readers. The book consists

of fourteen chapters, starting with general principles, a description of apparatus and theatre technique, followed by an account of traumatic lesions, and thereafter the different orthopaedic lesions are dealt with by delightfully brief but adequate descriptions of each. The whole volume is remarkably complete and there is little to criticize. Fractures are fully described and extraordinarily well illustrated, including such special fractures as fractured neck of the femur, fractured scaphoid, and excision of a fractured patella. The author does not detail the methods of reduction, as in the Colles's fracture, since this concerns only the surgeon. It is doubtful whether flexing the wrist, as advised by so many for maintaining the reduction of this fracture—the Cotton-Loder position—produces flexion-contraction of the fingers as is suggested. Diseases of bone are described in quite sufficient detail and the modern treatment of such of them as permit of treatment (e.g. rickets) is adequate. A good description of the treatment of tuberculous joints is given, although it is doubtful if a Thomas's hip splint is ever used now, but the modern method of ischio-femoral arthrodesis for tuberculous hips is described. The application of a Denis Browne splint in the treatment of a congenital club-foot is given in such detail that the nurse can easily apply it. The general impression is that the book, with possibly a few additions, would be quite sufficient for the medical student going up for his final examination. It is an excellent book and, being a Livingstone production, a delight to read.

Human Gastric Function. By STEWART

WOLF, M.D., and HAROLD G. WOLFF, M.D. With a foreword by WALTER B. CANNON, M.D. Oxford University Press; London Humphrey Milford, 1944.
Pp xv and 195 Figures 42 Price 25s

THIS is one of the most fascinating books in the whole realm of gastro-enterology. In the words of the subtitle, it is "an experimental study of a man and his stomach," the man being Tom, a fifty-seven-year-old Irishman who, at the age of nine, developed an oesophageal stricture as a result of drinking hot clam chowder. The subsequent operative treatment left Tom with a defect in his abdominal wall through which protruded a collar of redundant gastric mucosa. Through this opening he fed himself, first chewing the food and then spitting it through an ordinary kitchen funnel into the stoma. In spite of this handicap he remained in good health, pursuing a more or less normal life, and when he came under the observation of the

authors of this monograph his general condition was satisfactory. Tom was thus an ideal experimental subject, and his investigators took full advantage of the opportunity. Gastric motility and secretion and the vascular response of the mucosa were all investigated. The effect of various foodstuffs and drugs upon gastric function have also been investigated, but perhaps the most important, and impressive, section of the book is that dealing with the response of the stomach to emotional disturbances. Much of the information obtained was known before, but this is the most striking confirmation yet recorded of the close correlation between the emotions and gastric function. "I venture to declare that the functions of the stomach have never yet been investigated with the detailed care, the skill and ingenuity, that have been displayed in the researches carried out by the authors of this volume on the present subject." So writes Dr Cannon in his foreword. This is high praise, but not too high. This book can legitimately be described as a classic.

The Art of Medicine in relation to the Progress of Thought By A E CLARK-KENNEDY, M D, F.R.C.P. Cambridge The University Press, 1945 Pp 48 Price 2s

DR CLARK-KENNEDY'S thesis in this lecture, originally delivered in the History of Science course at Cambridge in the earlier part of this year, is that medicine should "be the connecting link reconciling the conflicting points of view of the humanities, on the one hand, and the sciences, upon the other." At many periods of history, medicine has made a valuable contribution to human thought, but in the present era it is not doing so. It lacks integration and a philosophy of life at the very time when this is all the more essential because of the growing power it is acquiring. Much has been written of the devastating effect upon civilization of the outpacing of moral advance by the tremendous advances of science: the machine is controlling man with results that have been all too obvious during the last six years. The same danger, according to Dr Clark-Kennedy, threatens in the realm of medicine, with a consequent risk of loss of intellectual balance. Medical education is "trailing along after a 'half-baked' materialism, already out of date." In the exposition of this thesis examples are drawn from the history of medicine from the time of Hippocrates. This is a thoughtful, if necessarily rather superficial, contribution to a problem that is vexing the minds of all thoughtful members of the profession, and particularly of those whose lot it is to be responsible for the education of medical students.

The Intelligent Parent's Manual
FLORENCE POWDERMAKER, M D,
LOUISE GRIMES London. W.
Heinemann (Medical Books) Ltd.,
Pp vi and 256 Price 10s 6d

THIS book, by the mother of several children and a medical practitioner familiar with psychological principles, yet able to steer clear of jargon, takes the reader through the phases of a child's development from infancy to adolescence, advising the parent at each stage how to deal with the inevitable pains and problems growing up. Nor do they neglect the joy of satisfaction to be found in the rearing of a family. A close day-to-day acquaintance with nursery gives conviction to the many illustrations drawn from real life with which the book is interspersed. The approach is practical rather than theoretical. On several points criticism could be made. The authors' views on feeding, for example, are not in conformity with the best-informed opinion in this country; it is a pity that the simple and expressive American title "Children in the Family" has been used in the English edition. However, let this deter the inquiring parent or educator, who will find in this book a little less intelligent, but a great deal more informative, knowledgeable, and written in a lively, entertaining style.

Arthritis What Can Be Done About It
By A E PHELPS, M D London. M.
Publications Ltd., 1945 Pp 94
Illustrations 12 Price 6s

IN the treatment of chronic conditions such as rheumatoid and osteoarthritis it is essential to obtain the intelligent cooperation of the patient. Few medical practitioners have time to spare to explain fully to the patient why and wherefore of his disease and its treatment. This little book from America sets out to explain in non-technical language why and how certain treatments are adopted and how the patient can help in his own treatment. On the whole the attempt has been successful, and the author manages to steer a passage between the extremes of undue optimism and pessimism. It is a pity that the old myths concerning diet in gout have been re-propagated. The only real criticism of the book is of the chapter on treatment: there is no justification for the statement "even those suffering from arthritis in severe form are curable. In fact a majority of them are cured." In this particular instance the difference between "cure" and "improvement" is so marked that to use the former when the latter is intended is unfair to the patient.

Principles of Physical Methods in Medicine
By G D KERSLEY, M.D., F.R.C.P. With
a foreword by FRANK D HOWITT, C.V.O.,
M.D., F.R.C.P. London William Heinemann (Medical Books) Ltd., 1945 Pp ix
and 85 Price 6s

In this little book Dr Kersley provides a useful introduction to a complex subject. Dealing in turn with electrotherapy, heliotherapy, roentgen and radiotherapy, remedial exercises, massage, hydrotherapy, and occupational therapy, he outlines the principles underlying the use of each form of treatment and its indications. Whilst X-ray therapy, radiotherapy and hyperthermia may claim, strictly speaking, to be aspects of "physical medicine," their use to-day is so specialized and, even in experienced hands, so fraught with danger to the patient, that inclusion in such a book as this is deprecated, the space allotted to them could have been devoted more usefully to a fuller exposition of massage. This book should prove of value to practitioners who wish to understand the whys and wherefores of physical medicine.

Symposia on Medicine and Surgery The
Medical Clinics of North America
London W B Saunders Company
1944.

THESE two symposia, one dealing with recent advances in medicine and the other with recent advances in surgery, have been reprinted by the United States Office of War Information from the *Medical Clinics of North America*, November and December, 1944. The articles are the contributions of different authors and cover many subjects of topical interest, including a well-illustrated article on refrigeration anaesthesia for amputations, another on plastic surgery, and an interesting discussion on confined air as a vehicle of infection.

NEW EDITIONS

In the preface to the second edition of *Acute Injuries of the Head*, by G F ROWBOTHAM, F.R.C.S. (E & S Livingstone Ltd, 30s), the author stresses the importance of closer cooperation between the general practitioner, the specialist, the government and industry in the treatment of civilian head injuries, in order that treatment up to rehabilitation may be continuous. A new chapter has been added on rehabilitation, in which the work carried out at the Castle of Callaly in Northumberland is described. The book, which is primarily written for the general practitioner so that he may adequately fill his important rôle in the team, is beautifully illustrated, containing in all 201 figures. Congratulations are due to both

author and publishers—to the former for his clear and illuminating exposition of the diagnosis, treatment, complications and sequelae of the different types of head injury, and to the latter for the really first-class production.

IN addition to a considerable amount of new material, twenty-six new illustrations have been added to *The Pathology of Internal Diseases*, by WILLIAM BOYD, M.D., LL.D., M.R.C.P. ED., F.R.C.P., Dipl. Psych., F.R.S.C., in its fourth edition (Henry Kimpton, 50s), a work already generously and beautifully illustrated. The additions are many, but mention may be made of sections on chronic disseminated tuberculosis, infective hepatitis, Meigs's syndrome, the Waterhouse-Friderichsen syndrome, the Rh blood factor in erythroblastosis foetalis, and a number of additions to diseases of the cardiovascular system.

As Physical Treatment by Movement, Manipulation and Massage, by JAMES B MENNELL, M.D., B.Ch., has been out of print for some time, the appearance of the fifth edition (J & A. Churchill Ltd, 30s) is particularly welcome. Much rewriting has been undertaken in its preparation and a number of new illustrations added. Two important subjects are included in the postscript, namely, asthma and adenoids, in both of which conditions physical therapy is now recognized to play a part in treatment. A separate chapter has been devoted to the ilio-tibial band, its anatomy, physiological function, pathology, and manipulation for restoration of mobility at the sacro-iliac joint.

A Handbook on Diseases of Children, by BRUCE WILLIAMSON, M.D., F.R.C.P., in its fourth edition (E & S Livingstone Ltd, 12s 6d) has been revised and brought up to date in all sections, in spite of the fact that only three years have elapsed since the appearance of the previous edition. A word of praise is due to the publishers of this well-known handbook, the production of which is particularly good for war time.

MUCH new material has been added to *Modern Methods of Feeding in Infancy and Childhood*, by DONALD PATERSON, M.D., F.R.C.P., and J FOREST SMITH, F.R.C.P., in its eighth edition (Constable & Co Ltd, 8s 6d). The section on vitamins has been entirely rewritten in the light of recent advances in knowledge, and the diets for sick children have been amended and a useful section on the overweight child included. This little book, which deals most adequately with all the problems of breast and artificial feeding, and the common ailments and illnesses of infancy and childhood, is a veritable mine of useful information, and the new edition will be warmly welcomed by the practitioner and all those engaged in the upbringing of the child.

NOTES AND PREPARATIONS

NEW PREPARATIONS

'ANETHANE' OINTMENT contains 1 per cent of the fat-soluble base of amethocaine hydrochloride, and has been prepared for the relief of pain from hæmorrhoids, skin diseases and allied conditions. The analgesic action is stated to last for two hours or longer. The ointment, which is issued in ½-ounce collapsible tubes, price 3s 6d (purchase tax 5d) is a product of Glaxo Laboratories Ltd, Greenford, Middlesex.

PROTEIN HYDROLYSATE, which for some time has been conserved for use in the treatment of starvation, is again generally available for the treatment of amino-acid deficiencies. A brochure dealing with the indications for its use and methods of administration has been prepared by the joint producers, Genatosan Ltd, Loughborough, Leicestershire, and Bengers Ltd, Holmes Chapel, Cheshire, and can be obtained on application to either firm.

STREPTOCIDE LOZENGES, each containing 1 grain (0.065 gm) streptocide (sulphanilamide-Evans) incorporated in a suitably flavoured base, have been prepared for the local treatment of affections of the throat and upper respiratory tract due to infection with organisms susceptible to sulphanilamide. The lozenges are issued in containers of 50 and 250 by Evans Sons Lescher & Webb Ltd, Liverpool and London.

ROYAL MEDICAL BENEVOLENT FUND

The Honorary Treasurer of the Royal Medical Benevolent Fund writes—"I recently received a letter from which I venture to quote

'For many weeks I have been intending to send the enclosed cheque for 50 guineas as a token of thanksgiving for the end of the bombardment of London, the preservation of my wife and myself and our home, and the cessation of the fighting in Europe.'

The Hon Treasurer continues—"If it was more widely realized how heavy and burdensome have been the lives of the beneficiaries of the Fund during the years of the European War, there would be many who, having a feeling of great thankfulness, would like by a 'token to the Fund' to bring greater comfort and happiness into the lives of these old people now that peace is again in our own land." Donations should be sent to the Hon Treasurer, Dr C Luther Bateson, Royal Medical Benevolent Fund, 1 Balliol House, Manor Fields, Putney, London, S W 15.

HOSPITAL DIET

A SECOND Memorandum on Hospital Diet, for consideration by hospitals, has been issued by the King Edward's Hospital Fund. There are many useful suggestions as regards catering and the staffing of hospital kitchens, and measures

for assuring the highest standard of cleanliness in such kitchens. The importance of salad measures for the conservation of the vitamin content of vegetables, menu planning and suggestions for menus, and the need for a hot meal for the night staff, are among the points stressed. The appendices contain, in addition to suggested menus, a number of useful recipes and tables relating to human nutrient requirements and the nutritive values of foodstuffs. A copy of the Memorandum can be obtained from Geo Barber & Son Ltd, Furnival Street, London, E.C.4, price 9d post free.

OFFICIAL NOTICES

The Sterilization, Use and Care of Syringes (Med Res Coun War Mem No 15) contains information on the choice and selection of syringes and needles, measures for sterilization and disinfection, for the prevention of contamination of injection fluids, for avoidance of infection following injections, and methods of mass inoculation. The memorandum is obtainable, price 4d, from H.M. Stationery Office. *Penicillin Ointments*. A note from the Ministry of Health announces the arrangements by the Ministry of Supply and three firms (Boots Pure Drug Co. Ltd., British Drug Houses Ltd., and Burroughs Wellcome & Co.) for a sterile ointment base to be supplied in 1 oz pots for the incorporation of penicillin solution. It stressed that the note refers to hospital dispensing only. *The Liver Extract (Regulation of Urine)*, 1945, dated July 19, 1945, again permits the use of injectable extract of liver without restriction as to the conditions to be treated and of oral preparations of liver on the prescription of a medical practitioner, but only for the treatment of pernicious and other megalocytic anæmias.

CONTENTS FOR OCTOBER, 1945

RECENT ADVANCES PART I

Medicine By A. P. Thomson, M.C., M.D., F.R.C. and John Malins, M.B., M.R.C.P.

Cardiology By William Evans, M.D., F.R.C.P.
Diseases of the Liver By Professor L. J. Witt M.D., F.R.C.P.

Pædiatrics By A. G. Watkins, M.D., F.R.C.P.
Arthritis and Chronic Rheumatism. By D. I. Collins, M.D.

Dysenteric Disorders By C. C. Chesterton O.B.E., M.D., M.R.C.P., D.T.M. & H.
Veneral Diseases By Col L. W. Harris D.S.O., M.B., F.R.C.P.

Tuberculosis By L. E. Houghton, M.D.

Child Health XVI—*The Care of the Crippled Child* By M. Forrester-Brown, M.D., M.S.

RECENT ADVANCES IN TREATMENT: MEDICINE

By A. P. THOMSON, M.C., M.D., F.R.C.P.
Honorary Physician, the United Hospitals, Birmingham

and JOHN MALINS, M.B., M.R.C.P.
Resident Medical Officer, the General Hospital, Birmingham

DURING the past year there has been no dramatic introduction of a new remedy to revolutionize treatment, but, with the more liberal supplies available, a great deal of work has been done to extend knowledge of the value of penicillin and thioracil. It was unfortunate that the supply of proteolyzed liver extract was interrupted soon after Davidson had published his preliminary and favourable report on its remarkable effect in certain cases of macrocytic anæmia which had failed to respond to liver extract and transfusion.

PENICILLIN

The field of activity of penicillin has been accurately charted by bacteriologists, and a direct study of the organism infecting a particular patient permits a confident statement from the laboratory whether or not it is sensitive, and it is true that, in general, bacteriological opinion of the value of penicillin is justified by the clinical results. But there are exceptions. As an example of these, subacute bacterial endocarditis may be cited, for it is frequently possible to rid the circulating blood of the *Streptococcus viridans* without affecting the course of the disease. Cases of chronic staphylococcal septicæmia and abscess formation, or with wandering thrombophlebitis, are not often cured by penicillin in the usual "systemic" dosage. Although the immediate effect is good, relapses occur. Penicillin acts by inhibiting the multiplication of bacteria, and disappointing clinical experience in proved cases of sensitive infection suggests several possibilities —

(1) The body may lack the power to destroy the infective organism although its multiplication is inhibited. When the influence of penicillin is withdrawn the organism may regain its activity.

(2) Vascular thrombosis, focal necrosis or other factors may provide bacteria with "safe areas" in which they are removed from contact with adequate concentration of penicillin over sufficient periods of time. Surgical experience with wounds involving local necrosis of bone is suggestive in this connexion, but in medicine one of the most important clinical groups in which bacterial "safe areas" are liable to be found is suppurative meningitis due to the pneumococcus, streptococcus and staphylococcus, adhesions in the pia-arachnoid may form rapidly and interfere with the diffusion of penicillin through the cerebrospinal fluid. Patients with this malady, who fail to respond quickly and completely to intrathecal injection of penicillin by lumbar puncture, should be immediately admitted to hospitals in which ventricular tapping can be undertaken for drainage and the introduction

of penicillin at a higher level. It has lately been suggested that block at the foramen magnum may be successfully overcome by the intravenous injection of hypertonic solutions. Ventricular puncture in experienced hands is so simple a procedure, however, that it would be unwise at present to rely on intravenous injections alone.

(3) It is possible, and indeed there is already evidence for it both from the laboratory and clinical study, that organisms may develop resistance to penicillin.

Three cases of troublesome recurrent ulceration of the mouth have been treated with penicillin and in all of them the clinical course was as identical as it was disappointing. The simple sucking of penicillin pastilles led in the first instance to almost magical improvement and the patients felt they were cured, within a short time they relapsed and renewed local application had but little effect. Systemic administration of penicillin was tried and failed, in one particularly severe case a second course of systemic treatment with large doses combined with diathermy to induce vascular congestion around the ulcers, also failed.

It is true that the cause of this curious condition of persistently recurring painful ulceration of the mouth in otherwise healthy persons is not known, but it seems likely that it is either due to a local deficiency in resistance to invasion or that it is the result of local allergy to some constituent of food. The dramatic improvement in the cases mentioned after the first local application of penicillin and the later failure suggest that the organisms of the mouth became in time insensitive.

Close study of a few cases of bacterial endocarditis has afforded more convincing proof of the development of bacterial resistance to penicillin. Dr A. L. Peene, clinical pathologist to the Queen Elizabeth Hospital, has kindly supplied the record of one.

The diagnosis was established not only by the usual clinical symptoms and signs, but by the constant recovery of *Streptococcus viridans* from the blood. The organism was sensitive to penicillin, systemic treatment led to its disappearance from the blood stream and culture twice weekly for several weeks were invariably sterile. There was concomitant clinical improvement and the patient went home. Two months later a relapse developed and the symptoms and fever recurred. Blood cultures again showed the presence of *Streptococcus viridans*, apparently identical with those obtained previously, but large doses of penicillin failed to make the blood sterile and positive cultures persisted up to the time of death. Laboratory testing showed that the organism *in vitro* had at least seven times its former resistance to penicillin.

Even greater proportional increase of resistance has been demonstrated in other cases of this sort. Better methods in the first administration of penicillin, in respect of dosage and duration, may eventually overcome the difficulty, but there is no doubt of its existence, and the fact that most forms of life have a remarkable power of adaptation to their environment does not make the conclusion surprising. For this reason the unrestricted use of penicillin by the public should not be encouraged. The price of freedom is eternal vigilance, and it may be that human tissues preserve their freedom from infection by constantly resisting it. Better it is, perhaps, to overcome an infection without assistance than to take penicillin "when it is sold at the grocers" every time the temperature reaches 100° F. Like sulphonamides, penicillin should only be used when the condition of the patient requires it. Of his condition the patient is rarely the best judge.

THIOURACIL

There is now no doubt that thiouracil is a valuable remedy for many cases of hyperthyroidism. When it was first introduced the dosage was often too large and toxic symptoms—fever, gastro-intestinal upset, a rash, enlargement of the spleen and leucopenia—were not infrequent, and these, with the extraordinary efficiency and safety of the surgery of the thyroid in skilled hands, restricted its use.

Early in 1944, beds in the emergency hospitals were denied to the civil population in preparation for D-day and cases of hyperthyroidism accumulated rapidly in the out-patient department. The sheer necessity of trying to do something for these patients led to the use of thiouracil again, but as they were out-patients, and as clinical supervision and laboratory control could at best be incomplete, only small doses were given—one tablet daily either of 0.2 gm. or 0.1 gm., depending upon the severity of the condition and the physique of the patient. The results in more than fifty cases have been surprisingly good but treatment must be maintained (usually with 0.1 gm. daily or every other day) and so far it has not been possible to discontinue it in more than a very few. Toxic reactions have been scarce, in the early cases there were some alarms over low white cell counts, but if the general condition of the patient is good these are of no serious significance. The tendency to leucopenia diminishes. Improvement is noticeable during the third week of treatment and is associated with a fall in the basal metabolic rate and a rise in the serum cholesterol. In a few cases the thyroid has enlarged but none developed symptoms of tracheal pressure. (Patients with large or intrathoracic goitres have not been treated.) In several patients auricular fibrillation returned to normal rhythm, but these took digitalis in addition to thiouracil.

Now the conditions of practice have improved and thyroidectomy is advised in young patients, in those with large or intrathoracic goitres, and in cases with serious temperamental instability.

Treatment with thiouracil will not remove a disfiguring goitre and the strain of long (perhaps, for all that is known at present, life-long) treatment is not advisable in the young and mentally unstable when surgery can offer such rapid relief. The most promising cases for thiouracil are those with latent "semile" hyperthyroidism. The patients treated have been allowed to get about quietly at home, even in the early stages of treatment, indeed, if they were not allowed most of them would have to! Mild symptoms of myxædema have occurred in a few but have rapidly disappeared with reduction of the dose of thiouracil, the risk is not a serious one if clinical supervision is reasonably good.

PROTEIN STARVATION

The tragedy of widespread famine in Bengal and later in Europe has directed attention to the problems of the proper treatment of cases of severe starvation. The work on protein deficiency, resulting from severe burns, fractures and other wounds, had already shown that it was impossible to make good the increased excretion of nitrogen in the urine, either by extra feeding of protein or by intravenous injections of different solutions (and in many cases it was demonstrated that the loss of nitrogen was out of all proportion to the apparent severity of the injuries). It was therefore not surprising that the intravenous injections of hydrolysates in the appalling conditions of the concentration camps in Germany were not as successful as had been hoped. There remains no doubt that the best remedy for malnutrition is good feeding, although it appears certain that in famine good feeding must be introduced gradually and the diet built up carefully.

One important practical result derives from the careful study of the blood proteins. Cohn has proved that it is in the globulin fraction that the immune bodies are almost exclusively found. By the use of globulin alone (and its separation

from the other constituents of the plasma is a matter of great difficulty) he has been able to protect susceptible children exposed to measles by a very small injective of 2 c cm of a concentrated solution

PRINCIPLES OF MEDICAL TREATMENT

The past thirty years with the indisputable triumphs of chemotherapy and the elucidation of many pathological mechanisms hitherto obscure have witnessed an astonishing improvement in the technical efficiency of practice. In periods of rapid progress of this sort, although knowledge comes, wisdom sometimes lingers, and it is pleasant to record that, despite inevitable preoccupation with therapeutic change, medicine has not lacked some who seek to transcend it and search for principles to guide them in the application of new discovery

Many there are who hold the simple faith that the medical problems of human sickness may be briefly stated in two sentences —(1) What is the correct diagnosis and (2) the discovery or the application of a specific remedy. But in the present state of knowledge it would be wise to admit that of the multitude who throng the consulting rooms of this country an accurate diagnosis is impossible, save in a very small proportion. Equally certain is it that the vast majority recover full health without effective treatment, if rest, reassurance and a placebo be denied that title. Medical teaching in the schools attaches primary importance to diagnosis and much of the wasted labour in the X-ray departments and laboratories of hospitals is due to futile search for the cause of symptoms. Were it not better to teach a student that, when confronted with a patient in whom neither history nor clinical examination warrant a diagnosis, his first duty is to decide, not on complete investigation in the ancillary departments, but whether or not the symptoms are serious (trivial although they may seem) and if they indicate some departure from the normal which is likely to be persistent, progressive and irreversible without treatment? Discretion of this sort should govern the pursuit of diagnosis, not only in the interest of the laboratories, where pressure of routine and unimaginative work may lead to dull resignation and despair, but also for the sake of the patient in whom the procedures of complete investigation may well give birth to the liveliest suspicion of grave disorder.

In men with wounds causing slight organic disability, at the end of the war of 1914-18, Hurst directed attention to the increase of hysterical symptoms which indubitably followed repeated and careful examination. Similar results are common in civilian practice. Radiological proof of osteoarthritic changes in the spine has converted vigorous men with attacks of transient lumbago into self-pitying valetudinarians who submit to repeated courses of massage, short-wave therapy, bathing at spas, vaccines and futile restriction of their diet and activity in the vain endeavour to cure a condition which others endure in ignorance without suffering and without complaint. Diverticulosis of the colon is not rare and it seldom causes symptoms, but its treatment often induces pernicious neurosis. Gastroscopy has revealed astonishing variations in the appearance of the mucous membrane of the stomach, new forms of gastritis have been described and treated. Many of them are physiological reactions to the nervous condition of the patient and the passage of a gastroscope may be disturbing to the man who suffers it.

Minor irregularities of the electrocardiogram have usurped the place of the cardiac murmurs which not so long ago condemned the healthy to lives of partial

invalidism It is not sufficiently appreciated that a single electrocardiogram rarely permits a decision as to the time of the development of an abnormality, it may have been present for years before its demonstration, and the precipitate conclusion that it is proof of the origin of recent symptoms may be disastrous It would not be difficult to find other examples of unnecessary alarm and treatment that have been the consequence of indiscreet interpretation of the results of intensive investigation, a cynic might take pleasure in the catalogue, but it is more profitable to seek the reasons for it That it exists, clinical experience during the last six years in England hardly permits a doubt. In that period, facilities for investigation have been restricted, treatment at times, and in certain areas for months together, has been limited to the care of the acutely sick, hardship and inconvenience there have been, and some avoidable suffering, but the public health has been maintained, a large number of invalids living sheltered lives on carefully planned diets with constant treatment of some kind or another have learned to their delight that they can eat ordinary food, dispense with drugs, mix on equal terms with their fellows and be happy

The spiteful allege that, so long as private practice persists and medical practitioners have a financial interest in both investigation and treatment, pecuniary consideration will bias judgement. Abuse of this kind is not common Much more often superfluous treatment and laboratory investigation derive from other motives a genuine desire to solve an intellectual problem, belief, misguided perhaps but often a strenuous conviction, in the value of particular therapeutic measures, charitable impulse to make sure that nothing that could possibly be helpful is left undone, or (and this is discreditable) sheer laziness—"these people want to be X-rayed Why stop them?"

The fault is one of critical judgement and is due to several causes Immature specialism promotes the study of viscera rather than the judgement of men

Clinical material in teaching hospitals contains so overwhelming a proportion of demonstrable and serious physical disease that it leads the student to believe that such changes are responsible for most symptoms, a short apprenticeship to a general practitioner in his final year would take him nearer to the truth

The cult of the theory of the single diagnosis breeds in the unwary a curious disposition to assume that the demonstration of an abnormality in a patient must in some way be related to symptoms previously inexplicable Most important of all, however, is the simple fear of being wrong Errors are inevitable, indiscriminate investigations in laboratories and X-ray departments will not avoid them—indeed they will increase them if the results are not controlled by clinical judgement and experience In the approach to treatment it is suggested that the first question to be answered is whether or not the condition of the patient merits either investigation or any treatment apart from reassurance The second problem is the significance to be attached to the discovery by "complete investigation" of an abnormality which is not immediately and obviously responsible for the symptoms

Trivial though at first it seems beside the therapeutic triumphs of recent years, a most valuable "advance" would be the rescue of the old idea that the treatment of a disease is not a satisfactory substitute for the care of a patient, which demands not only discretion in the pursuit of diagnosis, but a serious sense of responsibility in the prescription of treatment that restricts a happy and satisfactory way of life

CARDIOLOGY

By WILLIAM EVANS, M D, D Sc, F R C P

Assistant Physician to the Cardiac Department of the London Hospital

AS in other branches of medicine, the war has hindered the progress of research work in diseases of the heart, but it has not halted it altogether. Although startling discoveries have not taken place, useful additions have been made to the knowledge of diagnosis and treatment. It is intended here to recount these, to emphasize their application to clinical cardiology, and to point the way to other problems which might yield to further investigation. In such a survey there is a need to include older discoveries as well as a description of newer findings, and particularly those which from observation of current practice do not appear to be familiar to the majority of practitioners.

HEART PAIN

Views on *angina pectoris* have undergone a great change of late years, partly because of the description of cardiac infarction (coronary thrombosis) as a separate clinical entity, and partly because of the application of electrocardiography to the investigation of heart pain.

Even *terminology* applied to cardiac pain has become unstable for the same reasons. There is a feeling that the term *angina pectoris* is no longer an ideal one for in the light of increased knowledge it lacks definiteness in regards to pathology and pathogenesis, it also causes embarrassment when a practitioner discusses the illness with his patient or in the course of instruction to medical students in the hearing of the patient. It is suggested that heart pain might be considered as of two kinds, the one due to *cardiac infarction* and the other to *cardiac ischæmia*.

Cardiac infarction is preferable to coronary thrombosis for two reasons. The first is that in only about 60 per cent. of cases regarded clinically as instances of coronary thrombosis, is thrombosis actually discovered at necropsy, although cardiac infarction is present. Secondly, cardiac infarction in syphilitic stenosis of the orifice of the coronary artery by aortitis takes place in the absence of thrombosis. Cardiac ischæmia, as an alternative to *angina pectoris* of effort, expresses the mechanism of the pain and conceals from the patient the dread conveyed by the term "angina".

The *diagnosis* of heart pain in the presence of a normal cardiogram presents difficulties, for reliance must then be placed exclusively on the patient's history. The site of the pain cannot be accepted by itself as evidence of its coronary origin although a sternal distribution often supports such a view, similarly, its relation to effort is not decisive, although it is presumptive, of coronary disease. As the patient unfolds his story the technique whereby he describes the symptom may supply a clue. Thus, a tendency to emphasize, exaggerate, and even dramatize

the sensation he experiences, points to its non-coronary basis, and in this event the adjective used to describe the pain is likely to be one of the following —stabbing, pricking, shooting, knife-like, sticking, throbbing, niggling, burning or lancing. On the other hand, the patient with pain from coronary disease is inclined to minimize his complaint, referring to it as discomfort, ache, indigestion, tightness, constriction, or a sense of pressure, whilst describing his symptom calmly he lays his hand instinctively on his breast bone to indicate its seat.

Yet another error is common in diagnosis, twenty years ago too many cases with coronary artery disease (ischæmia or infarction) were regarded lightly as "windy dyspepsia." To-day, the guarded prognosis and restricted activities which belong to the management of coronary disease, are sometimes misapplied to a subject with innocent flatulent dyspepsia. Flatulence is common in heart disease, so that this symptom must not by itself determine the diagnosis. Clinical examination cannot decide and naturally the electrocardiogram is normal. Some help may come from a close questioning which may determine a longer duration of the pain, its close association with flatulence or with a meal, its occurrence sometimes at rest, and periods of freedom from pain. Some support for the diagnosis may come on cardioscopy while watching the progress of a barium swallow. Spasm of the lower end of the œsophagus causes delay of the thick barium paste, which occasionally recoils before its propulsion into the stomach when the spasm is relaxed by the swallowed air which distends the gullet above. Although these phenomena are present without causing symptoms, they are seldom absent in patients in whom dyspepsia simulates the pain of coronary disease.

The importance of these two groups has been shown, and some points in the differentiation have been outlined, but for a more ready recognition, the physical signs of each group need to be reinforced by the addition of others which are more reliable.

A group of patients with cardiac ischæmia shows an abnormal *electrocardiogram* similar to the one obtained in cardiac infarction. The explanation for this is not yet known, but it means either that an area of infarction is present, although small, or that portions of the myocardium are affected by ischæmic atrophy. In the meantime it needs to be emphasized that a patient subject to pain of cardiac ischæmia (angina pectoris of effort) frequently shows an abnormal cardiogram which is customarily regarded as belonging to cardiac infarction. This means that the test has become indispensable in the investigation of chest pain of doubtful origin or significance.

Three other pertinent questions need to be answered about the relation of the cardiographic test to heart pain —

- (1) Is it possible for a patient with recent cardiac infarction to show a normal cardiogram? If the test includes chest leads this is unusual, and much reliance can be placed on this.
- (2) Does the cardiogram of cardiac infarction ever recover? It seldom does, provided the tracing includes chest leads, although it must be admitted that in a few cases with recent coronary pain the abnormal tracing may recover quickly, but in such cases it is unlikely that the early changes actually stood for cardiac infarction.

- (3) Can the electrocardiogram of hypertension be differentiated from that obtained in a patient in whom cardiac infarction has been added to the existing hypertension? Admittedly this is difficult on cardiographic grounds alone. An intake of potassium salts accentuates the deformed T wave of cardiac infarction, but such a test has real dangers. Amyl nitrite, or tachycardia induced by exercise, more readily corrects the deformed T wave associated with cardiac infarction than the inverted T of hypertension, but such manœuvres are inconvenient and the test is not reliable. In the meantime the most dependable way of telling the difference is by observing the degree of T wave inversion in two chest leads, thus, if, when the T wave is inverted in lead I and other signs are equivocal, the inversion of T is greater in IVR than in CR₇, cardiac infarction is likely to be present, but if the reverse is true, i.e., greater in CR₇ than IVR, hypertension is the main underlying condition.

HEART SOUNDS

In the past, too little heed perhaps has been taken of heart sounds, and murmurs have attracted most attention. Neither accentuation nor attenuation of a sound can by itself prove of great value in diagnosis. It is now known that duplication of the first heart sound never occurs, and such auscultatory impression results either from the accentuation of the auricular or ventricular elements (*splitting*) of the first sound, or from the separation of these elements creating a triple rhythm. Splitting of the first heart sound is of great importance on account of its common incidence and the frequency with which it is mistaken for the presystolic murmur of mitral stenosis. Indeed, this is one of the most common errors which fosters unwarranted cardiac invalidism from the misinterpretation of an abnormal auscultatory sign. Splitting can be told from the murmur by its wider distribution (from the mitral area to the xiphisternum) and its greater intensity in the upright posture.

By *triple heart rhythm* is meant the cadence produced when three well-separated sounds recur in succeeding cardiac cycles. It has been known to clinicians in one form or another for more than half a century, but its significance even to-day is ill-understood. The reason for this is not far to seek, it is the outcome of a confused terminology arising out of an urge to explain the mechanism of sound production at a cost of neglecting to regard the disease which might cause an added heart sound to appear. A clinical classification of triple rhythm should deal with its cause in terms of heart disease and should deliberately exclude conjecture concerning the actual mechanism of the extra sound. When the position of the added sound in the cardiac cycle is considered alongside the clinical state in patients exhibiting triple rhythm it is possible to place them in three groups. As a rule, even under the handicap of severe tachycardia, the position of the adventitious sound can be told by auscultation, aided by the clinical data, and short of phonocardiography.

(1) *Addition of the third heart sound*—This auscultatory sign, when the added sound appears early in diastole and immediately succeeds the second heart sound, is found in young healthy subjects and in patients with right heart failure. Recognition of each variety comes from a regard of the site of maximum audibility.

of the sound, the effect of posture on it, and the healthy or diseased state of the heart. Thus, in the *innocent* kind the third heart sound is best heard a little internal to the apex beat. It is usually heard only in the reclining posture, and it is only found in young subjects, it is uncommon after twenty-five years of age and is never heard after the age of forty. The addition of the third heart sound as evidence of *right heart failure* is a valuable physical sign in the diagnosis of the condition. It presents as a clear sound in mitral stenosis, pulmonary embolism, failure in thyroid toxæmia or in anæmia, in constrictive pericarditis, and in certain congenital defects, notably auricular septum defect, the sound is present but less clear in hypertension, failure from emphysema, and in primary pulmonary hypertension. In mitral stenosis the third heart sound is often obscured by a mid-diastolic murmur. In all these conditions the triple rhythm is best heard over the displaced apex beat, and it persists with the patient in the upright posture, whilst it appears at any age. It bears repetition that the third heart sound in a patient over forty indicates right-heart preponderance, and one of the enumerated causes should be sought.

(2) *Addition of the fourth heart sound* —In this variety of triple rhythm the extra sound is added during auricular systole. In a proportion of cases the sound results from auricular contraction which is separated from ventricular systole on account of a delayed A-V conduction. Not all subjects whose P-R period in the electrocardiogram exceeds 0.2 second will show this *innocent* kind of triple rhythm, although in young subjects few will fail to do so. In a larger proportion of cases this type of triple rhythm is an expression of *left heart failure* from hypertension or, less commonly, from aortic incompetence. Here, although the added sound is not the direct outcome of auricular systole, contraction of the auricle is necessary for its production and, in every patient, it disappears with the advent of auricular fibrillation. Triple rhythm of left heart failure, although audible over the displaced apex beat, is usually heard best near the xiphisternum and, as it is accompanied by a palpable impulse, the rhythm is well appreciated by direct auscultation when the impulse is felt and the triple rhythm heard simultaneously.

(3) *Addition of a sound in late systole* —In this innocent variety of triple rhythm the added sound is nearer to the second heart sound than to the first and is no doubt comparable with the late systolic murmur which is also found in healthy subjects.

HEART MURMURS

Combination through the years, in patients presenting heart murmurs, of clinical auscultation and the tests of electrocardiography, cardioscopy, and often phonocardiography, has made it possible to allot to such murmurs a significance hitherto not possible. Two special advantages have come from such comprehensive study, namely, a more precise interpretation of the mitral systolic murmur, and the allocation to the innocent, or functional, variety of certain characteristics which facilitate its recognition.

Some four types of *innocent systolic mitral murmurs* can be readily identified by clinical examination. The most common, the *murmur of reclining posture*, is not loud and not long, and it is best heard in the reclining posture when a similar murmur appears in the pulmonary area. The innocent *murmur of upright posture*

is also common, as a rule this, too, is neither loud nor long, and it is best heard in the upright posture. Both murmurs are confined to younger subjects and are never met with after the age of forty. A third variety is the innocent *murmur in late systole*, it is not uncommon, and since it is always loud and long it is usually regarded as standing for organic heart disease. Its lateness in systole is readily taken on clinical examination because the murmur is nearer to the second sound than it is to the first. A fourth kind of innocent bruit, the *parasternal murmur*, is not rare. This, too, is loud and long, and is best heard in the fourth intercostal space at the left lateral border of the sternum. It differs from the murmur of ventricular septal defect in that there is no thrill, no cardiac enlargement, even on cardioscopy, and no abnormality in the electrocardiogram.

Unlike the first two, the last two types of innocent murmurs are found at all ages and are therefore a common source of error in diagnosis. Since nothing is known of the mechanism of these murmurs it is necessary to guard against theorizing about the cause under the pretext that this contributes in any way to the knowledge of the problem. Rather is it essential to be acquainted with the clinical characteristics of these murmurs and thus save the subjects that exhibit them, children and adults alike, from a life of unwarranted invalidism.

In regard to the long and moderately loud systolic murmur in the mitral area which is loudest in the reclining posture, it should become customary to refer to it in terms indicating the underlying disease, and not in words deputed to express mechanism. Thus, the *mitral systolic murmur of organic disease* (excluding hæmorrhagic murmurs) arises from mitral stenosis, aortic stenosis, aortic incompetence, hypertension, or when the heart is enlarged in complete heart block. In each of these conditions the murmur has no individual distinguishing marks on auscultation, so that the diagnosis must rest on the finding of other clinical signs, such as a third mid-diastolic or presystolic murmur in mitral stenosis, aortic systolic murmur in aortic stenosis, early diastolic murmur in aortic incompetence, a raised blood pressure in hypertension, and the characteristic bradycardia in complete heart block.

HEART FAILURE

Failure of the right heart, featuring cyanosis, distended veins in the neck, crepitations over the lung bases, distended liver, ascites, œdema of the ankles, and addition of the third heart sound, is easily recognized, but left ventricular failure with its paucity of physical signs frequently evades diagnosis during the early phase. During such a stage there is no cyanosis, no distension of cervical veins, no crepitations in the lungs, no enlargement of the liver, and no œdema of the ankles. How then is an early diagnosis of left ventricular failure to be made? It is only necessary to keep in mind that when a patient with a big left ventricle from any cause, notably hypertension, complains of nocturnal breathlessness, failure of the left ventricle is present, in such patients a triple rhythm from addition of the fourth heart sound is found near the xiphisternum, and pulmonary congestion on cardioscopy may be predicted with certainty. The need for early diagnosis of this condition comes from the satisfactory response to treatment by mercurial diuretics.

The mercurial diuretics—Since isolated fatal reactions to the different mercurial salts have been reported it is important to emphasize the rarity of such an event.

and to encourage the more general use of this eminently satisfactory form of treatment. Untoward results can be avoided if mercurial diuretics are never given intravenously in nephritis unless good response has been obtained in the first place by an intramuscular injection. Furthermore, when the diuresis from repeated injections in heart failure is diminishing, the frequency of the injections should be reduced, and never increased in the hope that such procedure will enhance diuresis.

The belief that *digitalis* is without value in the treatment of left ventricular failure with normal heart rhythm is an erroneous one. Indeed, it should always be used in such cases and in the anticipation of much improvement. Naturally, digitalis therapy should be combined with other methods of treatment, particularly mercurial diuretics.

BACTERIAL ENDOCARDITIS

Sulphonamides, with or without heparin, have proved disappointing in the treatment of bacterial endocarditis and a cure has only been achieved in isolated cases. Penicillin is still under trial, and, although it appears to have succeeded in many instances, there cannot be predicted for it as yet great curative qualities in the majority of patients suffering from this serious disease.

When bacterial endocarditis has been added as a complication in a patient with patent ductus arteriosus, *ligation of the ductus* holds out a good prospect for a complete cure. On this account, and in order to prevent progressive enlargement of the heart and heart failure, ligation of the ductus should become a routine procedure whenever the condition is diagnosed, and particularly when the patient is young.

CONSTRUCTIVE PERICARDITIS

Since a clinical syndrome has been described for this condition its common incidence has been recognized. Many of its signs are common to right heart failure and include cyanosis, distended veins in the neck, enlargement of the liver, ascites, œdema of the ankles, and triple rhythm from addition of the third heart sound. Breathlessness, however, is not as prominent as in other examples of right heart failure, whilst it is absent at rest, pulmonary crepitations are also absent as a rule and so are cardiac enlargement and murmurs. Confirmatory signs are obtained from the tests of electrocardiography and cardioscopy.

The relief of such symptoms following the surgical procedure of *cardiac decompression* encourages the search for the condition in patients in whom preliminary examination has provided evidence of right heart failure. The operation does not always produce the improvement expected of it, and investigation into the cause of this has shown that post-operative progress depends upon the degree of congestion cirrhosis which exists at the time of the operation, which in turn depends a great deal upon the duration of the illness. This is why the early diagnosis of constrictive pericarditis is so important; the early case responds well and immediately to cardiac decompression, whilst improvement in the late case is slow and incomplete.

DRUGS

Most of the drugs in common use in the practice of cardiology have been tested one against the other, under controlled conditions so that their respective merits are known from their clinical effects. Thus, for *rapid digitalization*, digoxin (3.0 mgm by mouth or 1.5 mgm intravenously) is the best preparation to use. For *continuous digitalization* there is no superior to the powdered digitalis leaf given as 1 grain, once, twice, or three times a day, according to need.

In the continuous treatment of *cardiac ischæmia* (angina pectoris) of effort no drug is expected to reduce the number of painful attacks, apart from anti-anginal remedies, notably mercury and iodide, in the syphilitic type. For the attack chewing a trinitrin tablet has no equal, but its action is seen at its best in prophylaxis and when the tablet is chewed immediately before undergoing some form of physical exercise which customarily brings on the pain.

Out of some thirty-eight active drugs with a reputation in the treatment of hypertension, none was found to exert consistent hypotensive effects, and a sedative medicine to allay the functional symptoms common to the condition is as yet the best form of medicinal treatment. Surgery, too, has failed to produce the beneficial results once predicted for it.

In *Stokes-Adams disease*, half a grain of ephedrine, given continuously three times daily, offers the best means of maintaining a raised heart rate, but it may fail to keep a patient free from the attacks if the heart rate is very slow. Should heart failure be added as a complication, digitalis may be given with benefit, because it does not affect the heart rate in idioventricular rhythm.

In *heart failure* needing mercurial diuretics, neptal, 2 c.cm intravenously, is the best to use, and the most effective form of premedication is provided by 30 grains of ammonium chloride by mouth, given as four sugar-coated tablets, two hours before each injection.

The easy acceptance of the unfounded claims made on behalf of proprietary remedies continues to mislead medicinal treatment. It is a stern criticism that trust in a host of potions without any proved value in the alleviation of heart disease but alleged to have a beneficial action on "the heart, blood vessels, or higher centres," is born of extravagant advertisements. Little organized attempt is being made to prevent this travesty of scientific therapeutics, and such can only be checked by the resolve of practitioners, individually, not to dispense any remedy unless the action attributed to it has been shown to be present during a controlled clinical trial.

DISEASES OF THE LIVER

BY PROFESSOR L. J. WITTS, M.D., F.R.C.P.

Nuffield Professor of Clinical Medicine, Oxford

BEFORE the treatment of acute hepatitis can be discussed, a brief account must be given of information which has been acquired in recent years on the etiology and pathology of acute catarrhal jaundice. There have been three major episodes of jaundice in this war.

The first was the outbreak of jaundice which followed the vaccination of American troops against yellow fever in 1942 (Sawyer *et al.*, 1944). The vaccine contained human serum which was proved to be the factor responsible for the jaundice. The lessons of this artificial pandemic are that the blood of apparently healthy men and women may contain the icterogenic virus or causative organism of catarrhal jaundice. So far as is known at present, this is the result of a previous attack of jaundice, although the infection may have occurred many years before or may have been subclinical. About 6 per cent. of young adults give a history of jaundice and are therefore potential carriers of the virus. Jaundice is known to have been transmitted by as little as 1/100 c. cm. of human serum and the resistance of the virus is comparable with that of the spores of bacteria. This type of jaundice has occurred after injection of convalescent measles serum, and also after transfusion of serum and plasma from the blood banks. It is called "homologous serum jaundice" (Ministry of Health, 1943) because it occurs only after the administration of human serum.

The second episode was the great increase in incidence of post-arsenical jaundice in 1942 and 1943. It is now believed that this was due to imperfect sterilization of the syringes at V.D. clinics and contamination with serum containing icterogenic virus. Presumably, carriers were present from whom the virus was transmitted to other patients at the clinics. MacCallum (1945) has demonstrated that the blood in post-arsenical jaundice contains the icterogenic virus, and post-arsenical jaundice is regarded as a variety of homologous serum jaundice. Unless careful precautions are taken, a similar type of "syringe jaundice" is liable to occur in any clinic in which many blood samples are taken or inoculations given, as in the control and treatment of diabetes, rheumatoid arthritis and tuberculosis.

The third episode was during the campaigns in Syria, N. Africa and Italy, and the high incidence of jaundice in the troops in successive autumns and winters. The symptoms of this epidemic jaundice were identical with those of catarrhal jaundice as it occurs in Great Britain. Here again a virus was detected (Cameron, 1943) and as a result the name infective hepatitis has come into use for the natural disease. Infective hepatitis, whether occurring in epidemics, or in the sporadic form hitherto known as catarrhal jaundice, has an incubation period of approximately twenty-eight days. Homologous serum jaundice has an incubation period of approximately one hundred days. Opinion has swayed to and fro as to the identity of the virus in the two conditions. At present, the majority of workers

believe that there is a single icterogenic virus, and that the long incubation period of homologous serum jaundice is due to the abnormal circumstances of infection.

Biopsies (Dible *et al*, 1943) and autopsies (Lucké, 1944) indicate that identical morbid anatomical changes are present in infective hepatitis, post-arsenical jaundice and serum jaundice. In all three there is a surprisingly severe hepatitis with destruction of liver cells. In all three there is complete absence of catarrh of the larger bile channels. The name catarrhal jaundice should therefore be abandoned. The terms used now should be "infective hepatitis," epidemic or sporadic, on the one hand, and "homologous serum jaundice," post-arsenical, post-vaccinal, or post-transfusional jaundice, on the other.

Knowledge that all these forms of hepatitis are due to a virus has made it possible to think rationally about prophylaxis. Infective hepatitis is usually a droplet infection, but the virus is also excreted in the urine and stools, and water borne infections have been described. Droplet infection is difficult to counter but excremental infection should be avoidable by good sanitation. Homologous serum jaundice can be reduced by avoidance of donors with any history of jaundice by careful checks on batches of human serum and plasma at the blood banks so that icterogenic batches can be promptly removed once they are detected, and by extreme care to avoid disseminating virus in clinics where large numbers of inoculations or venepunctures are performed. There is also evidence that pooled human serum contains an antibody which protects against infection by the icterogenic virus. This antibody can be concentrated in the gamma globulin fraction of the serum and can be used to protect individuals who are exposed to the risk of infective hepatitis or homologous serum jaundice (Stokes and Neefe, 1945).

TREATMENT OF ACUTE HEPATITIS

The treatment of hepatitis has recently been dominated by theories derived from experiments on animals, most of which have been performed during the last decade. It is too early to say how far these theories can be applied to disease in man, but such data as have been presented are not encouraging. The induction and prevention of deficiency diseases of the liver in animals, and the treatment of the prevalent diseases of the liver in man, do not appear to have a great deal in common. During this same decade the vitamin market in the United States has become saturated, and manufacturers have been looking for a new outlet for their productive resources. This has been found in the discovery that proteins may be split into amino-acids, and that these amino-acids may be used in therapeutics, whether as synthetic products or as complex protein hydrolysates. Technical and commercial enthusiasm in this new field of nutrition has created a hazy atmosphere of optimism about the treatment of diseases of the liver by nutritional principles, which is not altogether justified by the facts (Peters *et al*, 1945).

Fatty infiltration—In animals, fatty infiltration of the liver can be produced by high fat diets, or by pancreatectomy, which interferes with the assimilation of fat. Fatty infiltration eventually leads to cirrhosis of the Lænnec type, presumably by interfering with the nutrition of the cells. Experiments have shown that fatty infiltration can be prevented by pancreas, by lecithin or, finally, by choline, which is a constituent of lecithin and has the formula $\text{CH}_2(\text{OH})\text{CH}_2\text{N}(\text{OH})(\text{CH}_3)_3$.

The inference is that the body needs lecithin to transport the fat away from the liver, and it cannot manufacture lecithin unless it is supplied with choline

Fatty infiltration can also be prevented by good biological proteins, such as casein, but not by gelatin. Trial of the various amino-acids has shown that protein acts by virtue of methionine, which is one of the essential amino-acids. Methionine has the formula $\text{CH}_3 \text{S}(\text{CH}_3) \text{CH}_2 \text{CH}(\text{NH}_2) \text{COOH}$. The observant eye will note the methyl group (CH_3) which was also present at the tail-end of the choline formula, and it is now known that methionine prevents fatty infiltration because it provides the methyl groups for the manufacture of choline

Necrosis—So far the sequence of fatty infiltration and cirrhosis, and its prevention by lecithin and its precursors, have been discussed. Low protein diets have quite a different effect on the liver. They produce acute and subacute necrosis. This cannot be prevented by choline, but it can be prevented by methionine, and to a less extent by cystine and cysteine. These three amino-acids have the common property that they contain sulphur, and it is the sulphhydryl (SH) radicle which prevents necrosis. These same three thio-amino-acids exert considerable protection against liver poisons, such as chloroform and the organic arsenicals. All in all, methionine appears to be a key substance in the life of the liver, as it contains the labile methyl group, which protects against fatty infiltration and cirrhosis, and the sulphhydryl group, which protects against necrosis. Unfortunately, methionine is a difficult and expensive compound to synthesize. Cystine, on the other hand, can be prepared cheaply, but though it protects the liver against necrosis, it seems to encourage fatty infiltration and may be harmful in other ways.

In evaluating the physiological studies it should be noted that the effects of these biochemical substances have been studied in animals which were on grossly abnormal diets. Human diets rarely sink to such levels in temperate zones, although they unfortunately do in tropical and sub-tropical countries, where protein starvation is an important factor in the prevalence of diseases of the liver. Furthermore, the rôle of diet or dietary supplements is essentially prophylactic. There is no evidence that they can reverse an established cirrhosis or necrosis of the liver. Experiments on the treatment of subacute necrosis in animals (Bollman, 1943) indicate that excess of fat is undoubtedly harmful, but that a high carbohydrate regime is more beneficial than high protein.

Controlled trials of the value of dietary factors in the treatment of disease of the liver in man have been carried out in infective hepatitis, post-arsenical jaundice and homologous serum jaundice. The expectation of success was not very high, as the subjects were in a good state of protein nutrition and the liver in these diseases does not show fatty infiltration. Little or no success has, in fact, been attained. Darmady (1945) and Darmady and Hardwick (1945) have shown that there is no difference in the results of treatment of infective hepatitis with high or low protein diets. Groups of workers at Oxford (Higgins *et al*, 1945) and Cambridge (Wilson *et al*, 1945) have been unable to detect any therapeutic action of methionine in infective hepatitis. Peters and co-workers (1945) claimed a slight beneficial action for cysteine in post-arsenical jaundice, but it was not really of much clinical significance. Smaller scale trials with choline in infective hepatitis (Richardson, 1945) and homologous serum jaundice (Turner *et al*, 1944) have likewise been negative.

The *classical treatment of "catarrhal jaundice"* consisted in strict bed rest, together with a low fat diet, because the patient was unable to assimilate fat, and a low protein diet, because the metabolism of protein demanded work by the liver cells. It is doubtful if this old-fashioned prescription can be greatly improved. Strict rest seems to be more important than strict diet. The patient should be kept in bed until bile has vanished from the urine and the liver is no longer tender, being merely allowed up to use the lavatory. Convalescence should be gradual, and strenuous exertion should be forbidden for at least six weeks on account of the danger of relapse. As regards the diet, neither the fat nor the protein should be too low. A very low fat diet is unappetizing and in armies in the field it is usually impracticable. A very low protein diet seems undesirable in a patient who has to regenerate shattered columns of liver cells. Clinical experience has confirmed Bollman's (1943) conclusion from the treatment of animals whose livers had been damaged by carbon tetrachloride, that

"the caloric value of the diet should be as high as possible, and the ratio of carbohydrate and protein in the diet seems to be of less importance than the total caloric intake furnished by these substances."

The basic rule in the treatment of acute hepatitis is that the intake of fluid and food should be adequate to protect the patient from dehydration, acidosis, and tissue breakdown from malnutrition. The damaged liver is coping simultaneously with two tasks, the day-to-day needs of metabolism and the repair of its own substance, and it must be neither starved nor overburdened with material. A light diet with plenty of milk from which the top layer of cream has been removed fills the bill admirably. Self-selected diets also work out well, and it seems the patient will take no harm if he eats what he likes, whether he behaves like Jack Spratt or his wife. The real problem is when he does not want to eat at all. Turner (1944) believes that if the patient were given an infusion of dextrose for every meal avoided or vomited, some disasters might be obviated. Infusions of nitrogenous substances, such as plasma, protein hydrolysates and methionine, have been recommended in some quarters for the patient who is going downhill, but there is no published evidence of their value. There is no case for routine glucose and insulin (Lenz, 1944) and many patients find glucose nauseating. Nor is there any evidence that either liver extract or the water-soluble vitamins are useful, although it should be a general rule to supplement the diet with the fat-soluble vitamins A, D and K, if the amount of fat in the diet is much reduced.

DIAGNOSIS OF CHRONIC HEPATITIS

When a patient presents himself with persistent jaundice or ascites in middle or later life, great difficulty may be found in the differentiation of obstructive jaundice or carcinoma from intrinsic disease of the liver. The difficulty in ascitic patients is all the greater because pleural effusion, usually right-sided, is by no means rare in cirrhosis of the liver (Stewart, 1945). The distinction is important, because if the patient has an obstruction to the outflow of bile, simple or malignant, the sooner it is relieved by operation the better; if he has chronic hepatitis, operation may be harmful. The prognosis in cirrhosis, even with ascites, may be vastly better than in neoplastic peritonitis.

One simple clinical sign worth noting is the occurrence of *stellate nævi*, particularly on the face, hands and forearms. They are highly suggestive of cirrhosis. At first glance they look like flea-bites, but closer inspection shows a spidery structure with surrounding erythema. These cutaneous arterial spiders do not bleed, but they are often associated with telangiectases of the oral, rectal and nasal mucosa, which do (Bean, 1943).

X-ray examination is also of the greatest value. In chronic hepatitis the spleen is nearly always enlarged radiologically and can be seen indenting the stomach. The liver, on the other hand, is often shrunken and the space between pylorus and right diaphragm is reduced. Oesophageal varices can be detected in a surprisingly high proportion of cases of chronic hepatitis if they are looked for in the proper way (Kemp and Stewart, 1945).

The patient is examined lying down, a thick barium paste is used, and films are always taken. The varices produce characteristic grape-like filling defects. Oesophageal varices are found more than twenty times as often as the caput medusæ around the umbilicus.

Examination of the plasma proteins may be indispensable to the diagnosis. If ascites or pleural effusion is due to cirrhosis, the plasma albumin is always greatly reduced, to this rule there is really no exception. It is also possible to make the more general observation that in all chronic diseases of the liver the plasma proteins are usually altered in a characteristic way, the albumin falling and the globulin rising. Changes of this order are rare in carcinoma (Higgins *et al*, 1944). Finally, there is the prothrombin, which is also a plasma protein, although it is commonly thought of as a coagulation factor. Prothrombin may be reduced in any persistent jaundice. If the jaundice is due to obstruction of the bile ducts, the prothrombin will return to normal levels on treatment with vitamin K. If the hypoprothrombinæmia is due to intrinsic disease of the liver, it is usually refractory to vitamin therapy.

TREATMENT OF CHRONIC HEPATITIS

The treatment of chronic hepatitis can be considered under three headings, the parenchymatous damage to the liver, ascites, and raised portal pressure. Experience has led to the assumption that so long as jaundice is present in a case of chronic hepatitis, the disease is still active and progressive. In fact, jaundice colours the outlook and prognosis. It has always been customary to treat chronic hepatitis with a diet low in fat and high in carbohydrate, and to-day, in addition, a high-protein, high-vitamin intake is insisted on. It has hitherto been impossible to obtain any controlled data on treatment and all that it is possible to say is that patients do better on the more generous diets of to-day than on the Spartan fare of yesterday. In a small-scale trial Alice Stewart and I found no objective evidence that dried food yeast in the relatively high dosage of 1 to 2 ounces a day was beneficial, although the patients claimed a subjective improvement. Initial experiments with choline and methionine have been equally disappointing.

It has already been indicated that a fall in plasma albumin is one of the pathognomonic features of chronic hepatitis. By lowering the osmotic pressure of the plasma proteins, it favours the onset of ascites, and later of pleural effusion and generalized œdema. It would seem logical to treat this deficiency with a diet containing a large amount of good biological protein. Unfortunately, the experiment

is not successful. It is possible to maintain a patient with cirrhosis in positive nitrogen balance and actually to put flesh on him with high protein feeding, but the serum albumin does not rise. In other words, the patient has lost the power to synthesise adequate amounts of plasma albumin. Everything points to the fact that this is a function of the liver. For the same reason it is useless to inject large amounts of amino-acids or protein hydrolysates intravenously. Why not inject albumin itself, then? The difficulty is to get enough in appropriate form, although this difficulty is almost certain to be overcome after the war.

It may be illuminating to give some figures. Normally the plasma volume is 3 litres. Normally the albumin is over 4 gm per 100 c cm of plasma. In cirrhosis the albumin falls to 2 gm per cent. At first sight it would seem that only 60 gm. of albumin is required to repair the situation. Unfortunately, albumin rapidly diffuses out of the vascular system and only about one-thirtieth of the amount given remains in circulation. Therefore it would be necessary to inject 1,800 gm albumin or approximately 50 litres of plasma. This would be a Sisyphæan task. Fortunately it is now possible to fractionate and concentrate the plasma albumin and produce a 25 per cent solution of it. It seems likely that 7 litres of this fluid would restore the patient to normal, but the subject is still in the realm of theory because all such plasma as is available at present is going to the troops for the treatment of shock. Nevertheless, it seems possible that in the future it will be possible to treat the hypoproteinæmia and ascites of liver disease by substitution therapy with purified albumin injected intravenously.

Portal hypertension — The outlook is not so hopeful when the treatment of portal hypertension is considered. The most tragic cases are those in which liver function is well maintained but the patient has hæmorrhages from the distended œsophageal varices, which eventually lead to death. If the spleen is enlarged, the illness is diagnosed as splenic anæmia, but experience has shown that hæmorrhage is likely to recur after splenectomy. In two of my patients my colleague R. G. Macbeth has carried out the hazardous procedure of injecting sclerosing fluid into the veins through the œsophagoscope. In one of the patients, varices rapidly recurred but the other has remained well. Recently a case has been reported from America (Blakemore and Lord, 1945) in which the spleen and the left kidney were simultaneously removed, and the splenic vein was anastomosed to the left renal vein. In this way portal blood was shunted into the inferior vena cava and the pressure on the portal system was reduced. Such an operation may seem a surgical *tour de force*. It is only in recent years that radiological presentation of œsophageal varices has developed, and hardly enough is known of the natural history of the disease to recommend so drastic a remedy. Nevertheless, my own impression is that the patient who has bled from œsophageal varices lives under the continuous threat of a fatal hæmorrhage, and major operative procedures should not be feared if they hold out prospect of relief.

'CHOLECYSTITIS AND CHOLELITHIASIS

The only curative treatment of cholecystitis and cholelithiasis is operation. Nevertheless there are many cases in which operation is not desirable for one reason or another, and there is therefore a place for the medical management of biliary

disease In the past it has been customary to treat patients by drastic limitation of fat, on the grounds that fatty foods increase the cholesterol in the blood and thus favour the deposition of gall-stones Davidson (1944) has recently controverted this hypothesis vigorously, and has suggested that there is no proof that the cholesterol in the diet has anything to do with the formation of gall-stones On the other hand, fat is the normal stimulus for the discharge of bile into the duodenum and thus promotes the drainage of the biliary system. Finally, Davidson states that provided fried foods and indigestible types of fatty foods, such as pork and goose, are avoided, the patient with disease of the biliary tract tolerates natural fats, such as butter, milk, cream and the yolk of one or two eggs daily, quite well Davidson therefore recommends a diet of normal fat content, together with olive oil before meals, in the treatment of biliary disease

Chemotherapy—Biliary antiseptics of various kinds have been advocated in the past, particularly mercurochrome and hexamine There is no evidence that either of these is excreted in antiseptic form and concentration in the bile The case is different with the sulphonamides, which appear in the bile in the free form and in concentrations as high or higher than in the blood A medium or heavy dosage of a sulphonamide drug should therefore be of value in overcoming biliary infection If the drug is given for more than five days, or in repeated courses, the usual precautions must be taken against agranulocytosis and other toxic effects Penicillin is unlikely to be so effective, as infected bile so often contains *B coli*, which inactivates penicillin, but it may be worth a trial in difficult cases

References

- Bean, W B (1943) *J Amer med Ass*, **121**, 1412
 Blakemore, A. H., and Lord, J W (1945) *Ibid*, **127**, 748
 Bollman, J L (1943) *Surg Clin N Amer*, **23**, 1102
 Cameron, J D S (1943) *Quart J Med*, **12**, 139
 Darmady, E M (1945) *Brit med J*, **1**, 795
 —, and Hardwick, C (1945) *Proc Assoc Phys, Quart J Med*, **15** (in publication)
 Davidson, L S P (1944) *Edinb med J*, **51**, 184
 Dible, J H, McMichael, J., and Sherlock, S P V (1943) *Lancet*, **2**, 402
 Higgins, G., et al (1944) *Brit med J*, **1**, 211
 — (1945) *Ibid.*, **1**, 401
 Kemp, F H., and Stewart, Alice (1945) *Proc Assoc Phys, Quart J Med*, **1945**, **15** (in publication)
 Lenz, O (1944) *Acta med Scand*, **116**, 447
 Lucké, B (1944) *Amer J Path*, **20**, 471
 MacCallum, F O (1945) *Lancet*, **1**, 342
 Memorandum prepared by Medical Officers of the Ministry of Health (1943) *Lancet*, **1**, 83
 Peters, R. A., et al (1945) *Quart J Med*, **14**, 35
 Rennie, J B (1945) (personal communication)
 Richardson, J S (1945) *Brit med J*, **2**, 156
 Sawyer, W A., et al (1944) *Amer J Hyg*, **39**, 337, 40, 35
 Stewart, Alice (1945) (in publication)
 Stokes, J., and Neefe, J R (1945) *J Amer med Ass*, **127**, 144
 Turner, R. H., et al (1944) *Ann int Med*, **20**, 193
 Wilson, C, Pollock, R., and Harris, A D (1945) *Brit med J*, **1**, 399

PÆDIATRICS

By A. G. WATKINS, M.D., F.R.C.P.

Lecturer in Pædiatrics, Welsh National School of Medicine, Physician in Children's Diseases, Cardiff Royal Infirmary

PERHAPS the most valuable of recent advances in pædiatrics has been the recognition of the importance of the study of children in disease and health which has taken place in the last few years. Politicians as well as practitioners have shown their consciousness of the need for a better pædiatric service to the community and the whole matter has been given a fillip by the recommendations of the Inter-Departmental Committee on Medical Schools and by the report of the Royal College of Physicians on "Education in Pædiatrics." The Universities are interesting themselves in establishing departments of Child Health and the new Education Act has stressed the need for providing expert pædiatric services for children. All these are progressive signs and much welcomed, especially as the tendency is growing whereby the preventive and curative aspects of child health are being considered as part of the whole problem and not as separate water-tight compartments. We owe a debt, too, to our American colleagues who have visited this country with their Armed Forces and have stimulated our study in pædiatric problems and in the training of pædiatricians. Much remains, as will remain, to be done if all children are to have the benefits of a healthy life and in no branch of medicine is the prevention of disease more important, and the relationship between disease and social conditions more demonstrable, than in the care and study of the child in sickness and in health.

PENICILLIN

So many advances in the past year have been related to penicillin therapy that its use in children is worthy of special mention. Its action and general usage is the same as for adults, but in children it has special virtues, compared with sulphuramides, in the treatment of pyogenic infections, because of the absence of side-effects, such as nausea and vomiting, and in the difficulty in getting a small child to swallow large tablets—a point the practitioner appreciates perhaps more than the hospital resident. To offset this is the drawback to repeated injections, but these seldom cause real trouble, except the occasional formation of sterile abscesses at the site of injection. So long as penicillin is administered in hospitals this difficulty will not be a great one.

As so often with great therapeutic advances, interest is stimulated in underlying pathological processes, and it has been surprising to find how common is a positive staphylococcal blood culture, even in new-born babies. The staphylococcus is the most troublesome organism to deal with in the newborn, and penicillin has provided a much needed method of attack. The staphylococcus is responsible for skin sepsis, including pemphigus neonatorum, eye discharges and bone infection and is a source of infection to the mother, with a risk of breast abscess formation.

Epidemics of staphylococcal skin infection have been reported throughout the country during the last few years. Its presence in a nursery is a source of much trouble and difficult to eradicate.

There is no doubt as to the value of a penicillin ointment or cream applied locally in such conditions as pemphigus, skin sepsis, impetigo and infected eczemas, and penicillin cream or drops will soon clear both a gonococcal and staphylococcal eye discharge. Apart from the shortage of supply, which it is hoped is only a temporary measure, there is, however, the difficulty that the ointment retains its potency for a short time only. A carefully prepared ointment or cream will retain effective activity for about a fortnight at room temperature and for several weeks if kept in a refrigerator when not in use.

PATENT DUCTUS ARTERIOSUS

The results reported from America after ligation of the ductus have been encouraging and many cases have now been described in this country. Technically the procedure is not said to be too difficult, especially in children, and a child's reaction is remarkably slight. Here again, therapy has stimulated interest in the underlying pathology. The main reasons for performing such an operation are the relief of symptoms with prolongation of life and the prevention of subsequent infective endocarditis.

The diagnosis must be clearly established and the essential points are —

- (1) The characteristic continuous murmur over the pulmonary area
- (2) Dilatation of the pulmonary artery as shown radiologically
- (3) Increased pulse pressure at rest or after exercise
- (4) An accentuated or reduplicated second pulmonary sound

Some children seem to present no disabilities with this condition, which may only be discovered at a routine medical examination, but careful inquiry will generally show that there are some symptoms which have not been especially noticed. These consist in varying degrees of a sense of fatigue and a general reduction in vitality, a certain amount of breathlessness with, in some cases, occasional mild cyanotic attacks and sometimes a degree of infantilism. It is in those children in whom symptoms are prominent although vague that surgery should be considered. Moreover, a persistent patency of the ductus is always potentially dangerous because of the possibility of a supervening bacterial infection. In those cases in which the infective process is confined to the ductus the results of ligation have been dramatic, and with reports of an increasing number of patients with infective endocarditis cured by penicillin the prognosis in this formerly fatal disease is now much improved.

Ligation of the ductus should only be undertaken after most careful consideration of the case and by someone skilled in the operative and post-operative technique. Children are excellent subjects for it and the optimum age would appear to be between five and ten years old. The mortality in a growing number of cases reported would seem to be about 5 to 10 per cent., and a successful result means freedom from symptoms, prolongation of life, and the bogey of infection laid.

INTRA-TIBIAL MEDULLARY TRANSFUSION

This has proved to be a most valuable method for giving parenteral fluid to babies. The successful intravenous transfusion of fluid in a small baby is a skilled procedure and needs much practice. Tibial puncture is a relatively easy method and is no more difficult than a lumbar puncture. Saline, serum or plasma are given without difficulty by this route, but blood is often found to run too slowly because of its greater viscosity, and it has therefore a tendency to clot. Casein hydrolysate given intravenously has received favourable reports from America, and there seems no obvious reason why this, too, should not be given by the intramedullary route. Apart from the hæmolytic anæmias of the newborn there is little indication for blood transfusion in small babies, and plasma would appear to be the fluid of choice in dehydration, for which this method is mainly used. The danger is, of course, in the introduction of bone infection. I have had two cases in nearly one hundred tibial marrow transfusions, and in both there was a good response to penicillin, and the value of the fluid to the child was felt to be worth the risk. It is now my practice to inject 1000 units of penicillin just before the needle is removed, to prevent infection. The technique is as follows—

The skin of the tibia is carefully prepared as for any operation, the foot is everted so as to externally rotate the tibia, and the needle is inserted in the broad surface of the tibia about one centimetre below the tuberosity. Various types of needle have been described but the ordinary sternal marrow needle (Salah's) has proved the most satisfactory. The needle has to be forced through the bone and it enters the marrow cavity with a crunching noise. The correct position of the needle can be determined by withdrawing, through a syringe, bone marrow which is then forced back into the cavity. The needle is then joined up to the usual transfusion apparatus, and this must be done quickly to prevent clotting. Plasma tends to run slowly at first but the flow commonly increases in about ten minutes and is then regulated to between ten and fifteen drops per minute. The total amount needed is calculated as approximately 10 to 15 c cm per lb body weight, but larger quantities may be safely given provided the flow is slow, e.g., up to a pint of plasma in twelve hours. After withdrawing the needle the wound is sealed with collodion and a dressing applied to prevent contamination.

This method of giving fluid is often a life-saving measure which any practitioner should be able to do, given ordinary aseptic facilities.

GASTRO-ENTERITIS

This still ranks second to pneumonia as a lethal infection in infants, and, although the incidence has much lessened in the past years, it remains responsible for between 2000 and 3000 deaths each year. The etiology of the condition is not yet clearly defined. There are many who believe the primary cause to be a virus, whilst others hold the view that the majority of cases are secondary to a parenteral infection, especially of the upper respiratory tract, and of the ears in particular. A good deal of discussion has taken place recently in the medical press on the part played by ear infection. The association of otitis media and mastoiditis with gastro-enteritis has long been recognized. Post-mortem examination of infants dying of this disease shows pus in the middle ear in a high percentage of cases. It has therefore been suggested that all babies with diarrhœa and vomiting should either have a paracentesis or mastoidectomy done. The signs indicating ear infection are pyrexia, drum changes which are not always easy to detect, and enlarged glands in the

posterior triangle of the neck. The problem is not quite so simple as it sounds, as many infants show little or none of the above signs, and others develop an otitis, often with otorrhœa, secondary to the bowel infection. Although carefully selected cases may respond to mastoidectomy, this is too drastic a measure to advise in all cases, as some enthusiasts do. If the enteritis is secondary to an ear infection it would seem that in penicillin there is a method of attack which is less dangerous to the baby. I have used penicillin in such cases with apparent success—apparent because the assessment of therapy in gastro-enteritis is always difficult. Sulphonamides are not of great help in this way because of their poor absorption during diarrhœa and because of their failure to deal with the staphylococcus which may be the causative organism.

The essentials in the treatment of gastro-enteritis are still good nursing, parenteral fluid to combat dehydration, correct feeding, the treatment of any parenteral infection, in hospitals isolation to prevent ward cross-infection, and, lastly, prevention by breast feeding.

CÆLIAC DISEASE AND FIBROCYSTIC DISEASE OF THE PANCREAS

War conditions tend to bring about an increase in *cœliac disease* and this war has proved no exception. Most practitioners will have seen examples of this troublesome condition which is due to an unexplained mal-absorption of fat and to a lesser extent of carbohydrate. It has, however, been suggested by May and his colleagues (1941) that there is a nutritional defect present in which the vitamin B complex is involved, and they recommend the use of parenteral injections of B complex and crude liver extract and claim that with this treatment the child can soon tolerate a normal diet. Paterson and his co-workers (1944) in this country have described their results with this treatment, which they say gives an increase in height and weight with a quick loss of symptoms and an increased fat tolerance, and a more normal glucose tolerance curve. The routine they describe is as follows —

- (a) Normal diet suitable for the age
- (b) Intramuscular injections given into the upper arm on alternate days of vitamin B complex, 2 to 4 c cm, and concentrated crude liver extract, 2 c cm. The B complex is not easily obtained in this country, it is a Lederle product, distributed by Thackeray. The liver extract they use is Armour's "proethron forte". After a course of injections, which may have to be continued for from six weeks to four months, the B complex may be given by mouth as B-plex (Wyeth). Oral administration does not seem to be effective in the early stages of treatment.

These results await confirmation by other workers, but the method appears to be a valuable advance in the treatment of these difficult children.

Bananas, which were used extensively for *cœliac disease* in the good old days, can be obtained in dried form through the Ministry of Food, but the practitioner must provide a certificate stating the signs and symptoms of his patient, plus an analysis of fat in the stools. Bananas do not cure *cœliac disease* but they do afford a helpful way of giving protein and carbohydrate in an easily assimilable form, and if memory serves they are free from fat!

A more recently described disease which closely resembles *cœliac disease* in its general symptomatology and signs is *fibrocystic disease of the pancreas*. In this

condition there is fibrosis with cystic changes in the pancreatic ducts which is often only discernible by post-mortem microscopic examination. There is also an associated fibrosis of the lung, with sometimes bronchiectatic changes. Unlike coeliac disease there is a reduction in the pancreatic enzymes so that in any patient with suspected coeliac disease and chronic chest signs an estimation of pancreatic function should be made for differential diagnosis. The etiology of this condition remains in doubt but there is often a family history, and although it has been suggested that there may be a deficiency of vitamin A, this has not yet been fully proven. There is a high mortality death is usually attributed to broncho-pneumonia, and the real underlying pathology may not be discovered unless a careful microscopic examination is made at autopsy.

Treatment consists in giving a full diet to the child, who often has a good appetite in contrast to the true coeliac, with pancreatic preparations or predigested foods plus full doses of vitamins, especially vitamin A. Prevention of pulmonary infection is important.

THE RH FACTOR

Many reports have been made, and investigations carried out, on this fascinating problem during the past year. Although to the non-expert the intricacies of these new discoveries are puzzling, the main principles have been crystallized and the essential points for the practitioner to keep in mind are described below.

The clinical manifestations of hæmolytic anæmia of the newborn (erythroblastosis foetalis) depend upon whether hæmolysis takes place before or after birth, and if the former, there is likely to be either a macerated foetus with characteristic cirrhosis of the liver or an œdematous foetus, the so-called hydrops foetalis. If hæmolysis takes place after birth the common clinical picture is that of icterus gravis or, less commonly, of anæmia of the newborn. In addition to these clinical types there is usually a typical family history with a normal first child and increasing occurrences of the disease in any of its manifestations in subsequent pregnancies.

The father and the baby are both Rh-positive and the mother Rh-negative, and the baby must be given Rh-negative blood of a compatible ABO group. Approximately 200 c cm of either Rh-negative whole blood, or perhaps better, Rh-negative concentrated red cells, should be given by transfusion, and with this quantity a single transfusion usually suffices. The determination of the Rh reactions of the family is of more diagnostic significance than the erythroblastic blood changes which may be present or absent in the baby. Prompt treatment by the above method of babies born with this condition has saved many lives, although unfortunately, as yet, a method whereby its occurrence can be prevented has not been found.

References

- May, C, McCreary, J F, and Blackfan, K D (1941) *J Pediat*, 21, 289
Paterson, D, Pierce, M, and Peck, E (1944) *Arch Dis Childh*, 19, 99

DYSENTERIC DISORDERS

By CLEMENT C CHESTERMAN, OBE, MD, MRCP, DTM & H
Lecturer in Tropical Diseases, Middlesex Hospital Medical School

DYSENTERY is diarrhoea associated with the passage of blood and mucus. This article deals only with the two infective types, bacillary and amœbic dysentery. The most common causes of such symptoms in general practice in temperate climates are hæmorrhoids and carcinoma of the rectum. During the last twelve months, however, a great increase in the weekly notification of cases of infective dysentery has occurred. From an average of 150 to 200 in 1944, the figures for Great Britain are now 450 to 500 per week in the summer of 1945.

Among the Forces in the Middle East, dysentery continues to rank as the foremost cause of invaliding. This also applies to the Far East now that the successful suppressive treatment of malaria by mepacrine has been instituted.

BACILLARY DYSENTERY

Incidence—Although epidemics of amœbic dysentery do occur in tropical and temperate regions, the vast majority of epidemics are due to infection by one of the "Shigella" group, comprising four main types of *B dysenteriae*, the Shiga, Schmitz, Flexner and Sonne bacilli.

In the last war, cases of Shiga dysentery, the most severe type, accounted for as high a proportion as 60 per cent. of cases in certain epidemics. Not more than 25 per cent. of cases among troops in the Middle East have so far been due to this organism in the present war. There are indications, however, that in the Pacific area, Shiga infection, so common in Japan, may become more prevalent as troops come in contact with lands and installations fouled by the Japanese. Although rare and small Shiga epidemics are reported from time to time, the Sonne bacillus is most prevalent in the British Isles, whilst the Flexner type accounts for up to 60 per cent. of cases in the Middle East (Fairley and Boyd, 1943). The same is true of South Africa.

There can be no doubt but that the convalescent or chronic carrier from the Forces is a potential and actual focus of infection to the civil population. The danger is accentuated by overcrowding in houses, more communal feeding and inadequate staff in catering establishments and dairies.

In the United States, Weil (1943) reports that whereas the incidence of enteric fevers has fallen strikingly in recent years, "Shigellosis" has not done so, and he considers that, including mild and unreported cases, there are probably 700,000 cases annually. He states that the immediate vehicle of infection in the U.S.A. is usually contaminated food, especially milk and cream. Under Service conditions flies, water and direct contact, e.g. patient and attendant, are responsible for most infections. Newcomers are as usual more susceptible. Reinforcements rushed out

for the battle of El Alamein were only able to participate in that historic campaign thanks to sulphaguanidine, which must be ranked as one of the war winners

Summer diarrhoea—In Uruguay (Hormaeche, 1943), investigations have revealed recognizable dysentery bacilli in as many as 39 per cent. of a series of many hundred cases over a period of ten years. Organisms of the *Shigella* and *Salmonella* groups were found in 77·7 per cent. in all cases of enteritis in the second year of life and in 94·4 per cent. in the age-group two to twelve

DIAGNOSIS

Culture—Fairley and Boyd (1943) stress the importance of laboratory examination of absolutely fresh specimens, and as early in the disease as possible, i.e., during watery diarrhoea with flakes of mucus present. If a bedpan specimen is sent no disinfectant must be present. Once brown faecal matter returns to the stool the chances of successful culture are much less. A busy practitioner will find the rectal swab a convenient method. An ordinary throat swab will do, and can be passed direct or through a short length of $\frac{1}{2}$ -inch rubber tubing previously inserted in the rectum.

Excellent selective culture media are now available in the desoxycholate-citrate or S S agar. When laboratory facilities are not available on the spot a small portion of mucus collected from a fresh stool should be placed in a screw-top bottle containing a 30 per cent. solution of glycerin in normal saline, adjusted with sodium phosphate to pH 8 and tinted with phenol red. This will enable cultures to be obtained up to eighteen hours after passing of the stool.

Microscopy—Bacillary exudate in the early stages is typical. Clear mucus is tightly packed with cells. Red cells vary in number but are fresh and often in rouleaux. Polymorphonuclear cells predominate, but about 10 per cent. of large mononuclear cells with hyaline cytoplasm and even ingested red cells occur. The relative absence of mobility, even in the warm stage, helps to distinguish them from amebae.

Sigmoidoscopy is used in ideal conditions and in hospitals. Not merely does it give a definite indication of the diagnosis from the appearance of the bowel wall but affords the opportunity to obtain a direct swab for microscopy and culture.

TREATMENT

There is no objection to starting the treatment of any mild case of diarrhoea with the usual kaolin or bismuth mixtures, with or without small doses of chlorodyne or opium. Pending pathological examination, if dysentery is suspected on epidemiological grounds or blood and mucus are obviously present, it is wise to start giving one of the sulphonamides without delay.

THE SULPHONAMIDES have now practically replaced all other drugs. Scadding (1944) concludes that in mild cases the three common drugs, sulphadiazine, sulphapyridine and sulphaguanidine, are equally beneficial. Sulphathiazole is considered by Ferriman and Mackenzie (1944) valuable in severe cases as it relieves discomfort more rapidly. Hardy and Watt (1944), in the U.S.A.

have reviewed the use of sulphonamides in about 1500 civilian cases and their conclusions are —

Flexner infections responded very well, Schmitz infections were slightly more resistant, and Sonne cases and carriers were least satisfactory, although more responsive to sulphasuxidine

The relative merits of competing sulphonamides would appear to be as follows —

Sulphamylamide Effective though slower; danger to kidneys

Sulphapyridine as above, quicker, apt to cause nausea

Sulphathiazole effective, quicker action and less dangerous

Sulphasuxidine is the drug of choice in general practice when Sonne infections predominate

Sulphaguanidine is the safest because least absorbed, but for that reason dosage and cost are about treble It is the drug of choice in mass treatment, especially if this is ambulatory, e.g., under Service conditions

Dosage The first four mentioned above are given in four-hourly dosage of 1 gm after a loading dose of 2.5 gm The first dose of sulphaguanidine is 7.5 gm followed by 2.5 gm four-hourly Dosage of all sulphonamides is reduced after forty-eight hours, according to symptoms, but should be continued in diminishing doses until the fifth to seventh day

Drug prophylaxis —Marriott (1945) records the experience of American workers that recurring attacks of dysentery in a unit mean a high carrier rate and that the simplest way to stamp out the trouble is to treat all men, whether showing symptoms or not. They used sulphadiazine in a 2 gm initial dose followed by 1 gm twice a day for four days

PREVENTION

For the Forces in the field this problem resolves itself into control of water, faeces and flies Individual water-sterilizing outfits are provided to men in the forward areas Under desert conditions the Mosaic method of faecal disposal proved satisfactory

"Thou shalt have a paddle upon thy weapon, and it shall be when thou wilt ease thyself abroad, thou shalt dig therewith, and shalt turn back and cover that which cometh from thee." (*Deut*, 23, 13)

Fairley and Boyd report (1943) that covering faeces with a two-inch layer of soil was sufficient to prevent access of flies, yet did not prevent desiccation The fight against flies is now for them a losing battle sanitary squads with D D T sprays turn houses into fly traps, garbage into graves and latrines into gas chambers—for flies D D T will soon be an essential article of domestic use Painted on the electric light bulb or on one or two window panes it will banish flies from any room and fly-papers from the market.

Carriers are as important as in the enteric infections Hailwood (1944) reports an outbreak of Sonne diarrhoea affecting 32.8 per cent of the personnel of an artillery regiment, traced to a cook carrier who had suffered from mild diarrhoea a year previously Sulphaguanidine does not appear to be highly effective in sterilizing carriers, especially of the Sonne type, but Barker (1943) claims that sulphasuxidine in doses of 3 to 5 gm, four times a day for five days, is effective

Contacts—Hardy and Watt (1944) suggest giving contacts prophylactic doses of sulphadiazine, 1 gm twice daily, but point out the possible dangers of producing drug-fast strains by this method. Until more information is available on this most important point it would appear wiser to reserve the use of sulphonamides for proved or strongly suspected cases of bacillary dysentery, and to give such in adequate dosage.

Vaccines—Further efforts at producing efficient vaccine are reported, notably by Troitzky (1943) for oral administration, but their value is still uncertain and they are not in general use.

AMŒBIC DYSENTERY

Amœbiasis, or infection with *Entamœba histolytica*, may give rise in human beings to few or no symptoms. The dysentery which it generally produces, however, varies from a mild diarrhœa to cases as severe as in the bacillary disease. This article deals with bowel infection and makes no reference to the commonly associated hepatic amœbiasis or other complications.

Incidence—Military operations in Eastern India and Burma have been carried on under conditions which have led to large-scale amœbic infection of the troops with, especially in 1942, inadequate facilities for immediate and thorough treatment. According to Payne (1945), who saw 1000 cases in two years, amœbic infections were 50 per cent more common than bacillary.

Although there have been no serious epidemics reported among the civilian population of the British Isles, the military hospitals have been faced with great difficulties in the treatment of chronic cases, and discharged or undetected carriers may be a real source of danger. In the southern United States, an incidence rate of 14.1 per cent has been reported (Browne *et al*, 1945).

DIAGNOSIS

General ill-health and recurrent abdominal pain, especially after meals, sometimes, but not always, associated with diarrhœa, should arouse suspicion of amœbiasis (Taubenhaus, 1944). Tenderness over the cœcum, often mistaken for appendicitis and thickening of the colon, is a valuable diagnostic sign. As the differential diagnosis between amœbic typhilitis and acute appendicitis is often difficult, Morgan (1944) urges the employment of the Ochsner-Sherren regime in view of the undesirability of operating when active amœbic ulceration exists. An indurated mass in the rectum (amœboma) may be mistaken for a carcinoma. It disappears on treatment. Repeated faecal examination is stressed by all workers as essential. Specimens must be examined fresh—after a saline purge, if necessary. Faust's concentration technique for cysts is still in favour in the U.S.A., but doubt is thrown on the value of any other than direct and repeated stool microscopy by an expert (Adams, 1944). Charcot-Leyden crystals are a guide but not a sure proof and the exudate may be as highly cellular as in bacillary dysentery.

Proctoscopy—Payne (1945) reports that 50 per cent of cases show lesions in the rectal ampulla.

Sigmoidoscopy is now well established and as a rule is quite painless. By its use, and the subsequent microscopic examination of fresh scrapings from the bowel wall, an immediate diagnosis can be made in 80 per cent of cases.

TREATMENT

Emetine hydrochloride—Ever since Rogers (1912) introduced this drug it has continued to be used and abused. It should still be given by hypodermic injection as the first line of attack in cases seen early and showing vegetative amœbæ in stools or scrapings. Not more than twelve daily doses of from 1 to $1\frac{1}{2}$ grains should be given, and the patient should be confined to bed on account of tachycardia and muscular weakness resulting from its use. Emetine parenterally cannot reach the pre-cystic forms on the surface of the mucosa and about two-thirds of all cases relapse or become carriers, if treated only by injections of emetine. In an attempt to overcome this disadvantage, the firm of Eli Lilly has introduced "emetine euseals". These capsules, when taken by mouth, are supposed to liberate emetine in the large bowel, without unpleasant side-effects.

Emetine and bismuth iodide (E B I) is still held by most workers to be the best drug with which to follow up a course of emetine by injection. It is given in 3-grain doses in gelatin capsules, daily for twelve days. Pills, compressed tablets and enteric coated pills should be avoided. The patient should be confined to bed but on a fairly liberal diet. The nausea and diarrhœa which generally accompany its administration have led to the search for similar or alternative drugs. Auremetine, 1 grain thrice daily, is favoured by some, combined with bismuth carbonate, 60 grains in milk or soda water.

Although E B I has a much more potent effect in eradicating both vegetative amœbæ and cysts it requires to be supplemented by rectal medication.

Yatren, *quinoxyl* or *chimofof* are synonyms for oxy-quinolone-sulphonic acid combined with iodine. After a preliminary enema to wash out the bowel, 8 ounces of a 2.5 per cent. solution of chimofof are slowly introduced through a long rubber tube, with the patient lying on the left side. Every effort must be made to retain this for at least six hours.

Carbasone (stovarsol), containing 27 per cent of arsenic, has had a long vogue, probably because it is too easy to prescribe and not unpleasant to take. Its amœbicidal properties are, however, doubtful.

Combined treatment—Manson-Bahr (1944) reaffirms his belief that, after the preliminary course of emetine injections the combined treatment of E B I with retention enemas of chimofof, if properly given, is the most effective method. The enema is given in the morning and voided in the afternoon, and E B I, 2 grains, is given at night for ten days. Should a relapse occur, the course may be repeated and the strength of the chimofof enema increased to 4 or 5 per cent.

CHRONIC CASES—Failure of combined treatment to cure has been noted by many workers dealing with the emaciated cases repatriated from India and Burma. Adams (1944) considers that there is urgent need for research on new drugs. Lounie, in the discussion following the reading of Adams's paper, recalled the

theory of emetine-resistant strains of amœba, but Hargreaves (1945) considers this unproved and unlikely. He has published encouraging results in refractory cases which have failed to respond to all other treatment by the preliminary use of penicillin and sulphasuxidine.

Penicillin and *sulphasuxidine* apparently have no effect on the amœbæ, but an attack on the invading bacteria by these drugs has been found to produce such amelioration in the general condition of the patient—relief of pain, gain in weight—that a combined course with E B I and chiniofon can eventually be supported with satisfactory results.

Diodoquin (di-iodo-hydroxyquinoline) contains about 64 per cent of iodine as against 20 per cent in chiniofon. Craig (1937) first reported on its use, and since then many American physicians have acclaimed it as the best amœbicide (Hummel 1939). It has the advantage of being non-toxic and is easily taken by mouth in doses of 3–2 grains t.d.s., for twenty days. Recently, Morton (1945) has reported on its use in chronic cases from India and Burma. In three series he gave it alone with chiniofon retention enemas, and finally with chiniofon enemas and emetine injections. He obtained cures in approximately three-quarters of the cases after the first course in each series. He suggests that acute primary cases should be tried on six injections of emetine combined with three tablets of diodoquin t.d.s. for twenty days and compared with a similar series treated with E B I and chiniofon enemas.

If such a method proves effective it should greatly simplify the treatment of this too often refractory disease and reduce the time lost in hospital and in convalescence, with the tendency to relapse and the subsequent development of hepatitis.

References

- Adams, A. R. D. (1944) *Trans roy Soc trop Med Hyg*, 38, 238.
 Barker, D. S. (1943) *Amer J digest Dis*, 12, 443.
 Browne, D. C., et al (1945) *Gastroenterol*, 4, 154.
 Craig, C. F. (1937) The Effect of Diodoquin, etc. Report to G. D. Searle & Co.
 Fairley, N. H., and Boyd, J. S. K. (1943) *Trans roy Soc trop Med Hyg*, 36, 253.
 Ferriman, D. G., and MacKenzie, G. K. (1944) *Lancet*, 2, 687.
 Hallwood, J. G. (1944) *Brit med J*, 1, 806.
 Hardy, A. V., and Watt, J. (1944) *Amer J Pub Hlth*, 5, 503.
 Hargreaves, W. H. (1945) *Lancet*, 2, 68.
 Hormaeche, E., et al (1943) *Amer J Dis Child*, 5, 539.
 Hummel, H. G. (1939) *Amer J digest Dis*, 6, 27.
 Manson-Bahr, P. (1944) *Lancet*, 2, 718.
 Marriott, H. L. (1945) *Ibid*, 1, 679.
 Morgan, C. N. (1944) *Brit med J*, 2, 721.
 Morton, T. C. St C. (1945) *Ibid*, 1, 831.
 Payne, A. M. M. (1945) *Lancet*, 1, 208.
 Rogers, L. (1912) *Brit med J*, 1, 1424.
 Scadding, J. G. (1944) *Lancet*, 1, 784.
 Taubenhaus, L. J. (1944) *Naval med Bull*, 43, 521.
 Troitzky, V. (1943) *J Microbiol Epid Immunol*, Moscow, 6.
 Weil, A. J. (1943) *J Immunol*, 46, 13.

VENEREAL DISEASES

BY L W HARRISON, D S O, F R C P E D

*Adviser in Venereal Diseases, Ministry of Health, Consultant in Venereal Diseases,
British Postgraduate Medical School*

GONORRHOEA

DIAGNOSIS—There is no pathognomonic clinical sign of gonorrhœa, and are many other causes of discharge from the uro-genital passages than gonococcal infection. It would be interesting, for example, to have a series of analyses of the flora and fauna of the vaginal canals of "contacts" of males suffering from non-gonococcal urethritis, to relate them to the flora and fauna of the anal canals of the same contacts, and, finally, to relate all the findings to the use, by the contacts, of vaginal tampons during menstruation or for other purposes. Anyone who, like myself, has discovered in a stinking, retained menstruation tampon the cause of a foul vaginal discharge must rate such devices a potent means of fostering the growth of intestinal organisms in the vagina.

In *staining smears of discharge*, fruitful sources of error in diagnosis are trust in a single stain and poor technique in practising the Gram method of staining. As regards the use of a single stain, Barritt (1944), in an addendum to a recent memorandum on his modification of the Pappenheim stain said, "a bacteriologist in the Royal Navy has written me his appreciation of the stain, and has remarked that he stains directly with it and not as a counterstain in Gram's method." The latter remark is unfortunate. Barritt's stain, when properly made, is excellent for surveying the cells and the micro-organisms in any smear of discharge from the uro-genital passages, but reliance on it alone, or even its use as a counterstain unless it has been made with great care, could lead to many false diagnoses of gonorrhœa. For counterstaining in Gram's method I know nothing safer than 0.2 per cent. neutral red, to every 100 c cm of which has been added 0.2 c cm of a 1 per cent. solution of glacial acetic acid.

A method of diagnosis appropriate to all cases of urethritis, other than straightforward acute cases of gonorrhœa, is examination of specimens in the fresh state between slide and coverslip under a low power objective, such as one-sixth. If secretion from the prostate and seminal vesicles is first examined in this way, it may not be necessary to stain and search dried films, since in a few seconds it may easily be seen in the wet specimen that it does not contain a pathological number of leucocytes. The same applies to examination of the centrifuged deposit of the urine, which should never be omitted, such an examination may reveal the cause of a urethral discharge in the form of irritant crystals, such as calcium oxalate.

CHEMOTHERAPEUTIC PROPHYLAXIS—Jones (1942), Kline and Ryan (1942), Loveless and Denton (1943) and others have shown clearly that sulphathiazole or sulphadiazine, taken in adequate doses not later than the day after exposure, can prevent gonorrhœa without masking a concomitant syphilitic infection. A suitable dosage appears to be. 2 gm as soon as possible after the risk,

[Received for Publication, July 30, 1945]

2 gm at bedtime, if this occurs more than two hours later on the same day, and 5 gm the following day, in three doses. The general adoption of such a method for the prevention of gonorrhœa in large bodies of men, such as those in the Services, raises questions of effects on coordination of hand and eye, sulphonamide sensitization, and so forth, but for use in individual cases, when a practitioner is asked to do something to prevent infection following a risk already taken, there can be no doubt that this method should receive first consideration.

CURATIVE TREATMENT—Penicillin—To-day, the first line of attack on a gonococcal infection is by *penicillin*. An important consideration governing the dosage is the fact that gonococci can be trained *in vitro* to resist penicillin, and the development of penicillin-resistant strains by underdosage should be prevented by every means possible. The dosage which has been recommended by different workers has ranged from 50,000 to 200,000 units, or more, that recently recommended by myself to directors of venereal diseases treatment centres in this country is 30,000 units every two hours, for five doses. This recommendation was drafted and circulated without knowledge of the recent article by Lloyd Jones, Martland and Allen (1945a), in which it was reported that 265 cases of gonorrhœa had been treated in this way with only one failure. It is possible that the time over which a dose of 150,000 units dissolved in water is administered in the treatment of gonorrhœa could be reduced to less than eight hours, but it seems inadvisable to try any reduction of the total dose.

Romansky *et al* (1944, 1945) have found that by suspending penicillin in a mixture of peanut oil and beeswax the remedy can be maintained in the blood for an average of seven-and-a-half hours after injection of 100,000 units, and for ten hours after 150,000, the average durations in the urine after these doses were twenty-four and thirty-two hours, respectively.

Of 100 male patients with acute gonorrhœa who were treated each with a single injection of 100,000 units, all but seven were cured, and these responded to a further injection of 150,000 units. Of 75 treated each with a single injection of 150,000 units, all were cured. The details of progress show decided differences between the two doses. Thus, of 100 treated with 100,000 units, 48 showed a change to mucoid discharge in six hours, but of 75 treated with 150,000 units, 46 showed this change in the same time. After the smaller dose, 79 per cent were bacteriologically negative at the end of seven hours, after the larger dose over 82 per cent were negative. The authors report dramatic amelioration of symptoms and signs in eleven cases of acute prostatitis and three of acute epididymitis in the above series.

Zinnamon and Seeberg (1945) have successfully treated gonorrhœa in the female with single injections of 150,000 units suspended in sesame oil and beeswax. Unfortunately, at the time of writing, these methods of suspending penicillin have not been developed sufficiently in this country to permit of the single injection method of treating gonorrhœa being generally adopted. In the event of the first total dose failing, whether given by one or a number of injections, further administration of the same remedy in double the first total dose is advisable. The administration of sulphonamides with this second course is worth consideration.

It is too much to expect that the high degree of success (over 90 per cent) which has hitherto been reported in this form of treatment will be maintained, since the disappearance of strains of the gonococcus that are sensitive to penicillin must lead to an increase in the percentage of resistant strains. It may not, however, be unduly optimistic to expect that with the reduction of fornication in this country

consequent on the ending of the European war, resistant strains will not be distributed about the country at such a rate as if penicillin had been available earlier

Penicillin is also a remedy for syphilis and its use in gonorrhœa raises the question of its masking a concomitant infection with *S pallida*. Examples of its effect in prolonging the incubation period of syphilis have been reported by Van Horn and Dakin (1944), by Shafer and Zakon (1944), and by Osmond (1945). Because of this, in all cases of gonorrhœa which have been treated with penicillin the blood should be tested for syphilis at intervals during a subsequent period of not less than six months

Good effects of the local application of penicillin in gonococcal and other forms of ophthalmia neonatorum have recently been reported by Sorsby (1945), who found that the best method was to instil the remedy in a strength of 2,500 units per c cm into the conjunctival sac every five minutes until discharge had ceased, then half-hourly until the sac was "dry," hourly for twelve hours, and two-hourly for the next twenty-four hours

Although it is impracticable here to discuss *sulphonamide therapy* of gonorrhœa, which must already be sufficiently familiar to readers, it may not be out of place to mention what the routine use of sulphonamides in ophthalmia neonatorum has accomplished in the prevention of blindness. In the five years 1934 to 1938 the total number of notifications of ophthalmia neonatorum in England and Wales was 21,326, from which 157 infants emerged with impaired vision and 38 blind. In the five succeeding years, during which sulphonamide treatment became established as a routine measure, 19,696 cases of ophthalmia neonatorum were reported, and of them 55 (24 in 1939) emerged with impaired vision and 9 blind. With regard to the numbers of notifications, it is of course well known that only a relatively small proportion of cases of ophthalmia neonatorum are due to the gonococcus but this organism occupies a prominent place in the microbiology of cases resulting in blindness

VENEREAL WARTS

Following the report of Culp, Magid and Kaplin (1944) recording the good results of treating venereal warts with a 25 per cent. suspension of podophyllin resin in liquid paraffin, Macgregor (1945) has reported similar success in twenty-five cases

The suspension was well shaken and applied liberally to the affected areas, care being taken to bring, and keep, it in contact with all portions of the growths, a small orange stick was useful in getting the paint applied between the growths. The application was washed off after six to eight hours, the part thoroughly dried, and then dusted with compound zinc powder to prevent inflammation

Haber (1945) found that this method was apt to be followed by troublesome inflammation of the treated areas and modified it by using 5 per cent. podophyllin in tannic acid. For one or two days before starting the podophyllin treatment the parts were bathed frequently with warm eusol or saline and immediately before the application the normal parts of the area were protected with a thin layer of zinc ointment. The podophyllin mixture was washed off after eight hours and the treatment was repeated the following day. If further treatment was required beyond the second day, the routine procedure was to wash with eusol and then apply tannic acid powder, but apparently further applications of the podophyllin mixture might be made after a lapse of two days. In this way thirty-five cases were cured in an average of four to five days

CHANCROID

The sulphonamides—Greenblatt *et al* (1943) have carried out some valuable experiments by inoculation of nineteen volunteers with *H ducreyi*. They found

that the most successful ointment to prevent infection after inoculation was a 25 per cent mixture of sulphathiazole or of sulphadiazine in a water-soluble base. Oral administration of sulphathiazole immediately before, and for two or more days after, inoculation was successful in preventing the infection, the usual daily dose was 5 gm. In control cases the typical lesions following inoculation responded well to oral administration of sulphonamides.

SYPHILIS

DIAGNOSIS—*Lumbar puncture*—The annoying tendency of a lumbar puncture needle to deviate from the middle path may be prevented by inserting it with its bevel facing the head or the feet of the patient, like a carpenter's chisel, the needle tends to travel away from its bevel.

False serum reactions—It is often forgotten that a positive reaction to a serum test for syphilis, even when repeated, should not forthwith entail a diagnosis of syphilis. The increase in the practice of including such a test in general health examinations has brought to light a number of hitherto unsuspected conditions which may cause false positive reactions to serum tests for syphilis, and amongst those mentioned in a recent discussion (Harrison and Osmond, 1943) malaria, glandular fever, vaccination, typhus fever, atypical pneumonia and pregnancy have unusual importance at the present time, especially as the reactions may persist for some months. Many, however, doubt the tendency of pregnancy to make the blood positive. My own view, which is based on over twenty years' observation of the tests carried out in laboratories approved for this work under the national venereal diseases scheme, is that, whereas a good method is unlikely to give false positive reactions in pregnancy, a faulty method (of which there are still many in this country) is more likely to give false positives with pregnancy sera than with normal ones. On this point there is good supporting evidence in the League of Nations reports (1924) by Madsen and by Milinska on special serum testing carried out in laboratories in Copenhagen and Warsaw between the League's Serum Conference in Paris in 1922 and that in Copenhagen in 1923. The lesson is that when a pregnant woman's blood has given positive reactions to the usual serum tests for syphilis, but there is no other evidence of syphilis in herself or her family, she should not forthwith be classed as syphilitic. In such a case the blood should be tested in one or more other laboratories. If these also report positive reactions, the question of a diagnosis of syphilis and consequent treatment is one which should be decided by consultation with experts.

TREATMENT—*Arsenical and bismuth remedies*—*Post-arsphenamine jaundice* is a complication of treatment which occurs almost exclusively in cases dealt with in service and civilian treatment centres. The suggestion of the Salvarsan Committee of the Medical Research Committee (now Council), that an infective factor plays some part in the causation, has received great support from MacCallum (1943), Salaman *et al* (1944), Sheehan (1944) and others, who suggest on strong grounds that the infecting agent is passed from patient to patient through the medium of the syringes. Bigger (1943) showed conclusively that the methods of sterilizing syringes employed in many treatment centres were inefficient, and it is clear that when a number of patients have to receive intravenous injections from the same syringe at short intervals, nothing less than adequate boiling of the syringe and

needles between any two injections is sufficient to guard against the danger of transmitting the infecting agent. Since the type of jaundice under discussion is so rare in private practice, and the space here is limited, treatment of the condition cannot be discussed, but it may be said that after recovery it is permissible to resume arsenical treatment.

Arsenical encephalopathy is a highly fatal complication of arsenical treatment of syphilis which is fortunately rare under what may be called the prolonged systems of treatment mentioned below. Ransome, Paterson and Gupta (1945) report brilliant results from nursing the patients in the sitting position, a method which they have found successful in malarial coma. This position reduces the intracranial capillary pressure to nil, thus favouring reabsorption of fluid from the cerebral tissues.

The treatment is started with lumbar or cisternal puncture, which is repeated if the coma seems to deepen. Fits and restlessness are prevented by full use of hexobarbitone followed by paraldehyde, or sodium phenobarbitone, 6 grains intramuscularly, the authors lay particular stress on the prevention of fits, which increase the cerebral oedema.

SCHEMES OF TREATMENT—For comparison with recent alleged advances in the arsenical and bismuth treatment of early syphilis it may be convenient here to outline briefly some of the systems which they were designed to supersede.

The Gennerich system—One of the finest reports on the treatment of early syphilis with arsenical and mercurial remedies was that of Gennerich (1914), a naval surgeon stationed at Kiel, who was able to keep an unusually large proportion of his patients under subsequent observation for long periods.

The article reported results of treatment with salvarsan and mercury by different systems, dating from the first use of salvarsan in 1910, during three successive periods. In the last series all patients had been treated between March 1912 and March 1913, so that at the time of writing none had been under observation less than a year; the observation was by blood tests and examinations of the spinal fluid. In this last series, primary cases received at most eleven injections of old salvarsan, totalling 4.4 gm. (equivalent in arsenic to 5.8 gm. neoarsphenamine), and fifteen injections or less of calomel, totalling $7\frac{1}{2}$ to 12 grains in two months. Secondary cases received at most 6 gm. salvarsan and 12 to 18 grains of calomel in a maximum period of four months. Of 162 cases of early syphilis (92 primary and 70 secondary) treated under this scheme, 95 per cent. were reported to have shown satisfactory results.

During the last war the routine treatment given to soldiers was similar in amounts of arsphenamine to that given by Gennerich to his primary cases, and this may explain why so few soldiers treated then for early syphilis seem to have reported later at the civilian venereal diseases clinics with late effects of syphilis.

The intermittent and alternating systems—Between the two wars the amount of treatment considered necessary for early syphilis gradually increased, and in this country the system which persists in most civilian treatment centres is based on the "Plan of Intermittent Treatment" recommended by the League of Nations Committee of Experts on Syphilis and Cognate Subjects (Harrison, 1935, Martenstein, 1935). It consists of four courses of neoarsphenamine and bismuth, each consisting of ten weekly injections of neoarsphenamine, totalling about 5.8 gm., concurrently with the same number of a bismuth compound, totalling 2.0 to 2.4 gm. bismuth metal. The intervals between courses are from three to five weeks, and the whole treatment lasts approximately forty-eight weeks. In the U.S.A. until recently the scheme mostly practised has been that shown in the same committee's "Table of Alternating Continuous Treatment of Early Syphilis,"

which is based on the recommendations of the well-known Cooperative Clinical Group of the U S A. In this scheme the arsenical and bismuth courses are for the most part given separately, and generally speaking the treatment is much less intensive than that mostly practised in this country, considering that here 23 gm. neoarsphenamine and 8 to 9 gm. bismuth metal are given in about forty-eight weeks, but in the long treatment of the U S A only 18 gm. neoarsphenamine and 4.5 gm. bismuth metal are given in sixty-nine weeks.

For the American alternating system a cure rate of 85 to 90 per cent is claimed. Unfortunately there are no elaborate analyses of the results of the British system of intermittent treatment with which to compare the American figure, but I am confident, from my knowledge of the work of the different clinics in this country, particularly the great rarity of clinical relapse in patients who have undergone the intermittent treatment outlined above, that such an analysis would show much more satisfactory results. Indeed, this is to be expected when consideration is given to the results claimed by Gennerich for a treatment which in the main was very little more than that given in only one of the British courses.

The short intensive system—Results of intensive treatment of early syphilis which are reviewed below add conclusive evidence to that advanced by myself in *The Practitioner* (1931), that in early syphilis the concurrent administration of arsenical and bismuth remedies affords results far superior to those following administration of the two types of remedy in separate courses.

The difficulty of getting patients to persevere with the long programme of treatment prescribed in the U S A, and the urgent need to complete the treatment as quickly as possible, which has been dictated by war conditions, have increased interest in the short intensive schemes re-introduced by Hyman, Chargin and Leifer (1939). These workers first treated a number of early cases of syphilis with neoarsphenamine administered by the intravenous drip method on ten hours of each of five successive days, to a total dose of 4.0 gm. The results as reported by Leifer, Chargin and Hyman (1941) were satisfactory in 89 per cent of cases that had been observed sufficiently long. The toxic effects were, however, much too serious and numerous to permit of the method becoming a routine procedure, and the authors discarded neoarsphenamine in favour of mapharsen, which is the hydrochloride of *m*-amino-*p*-hydroxyphenylarsine oxide. The use of this remedy, given by the same method in a total dose of 1.2 gm. in five days, resulted in 82 per cent of 99 cases giving satisfactory results. Of 138 cases receiving less than 1.2 gm., only 79 per cent showed satisfactory results.

In the mapharsen series there were fewer toxic effects but these were still far too serious and numerous, and many workers have introduced modifications mainly designed to make the method safer without reducing its therapeutic efficacy. The results of some of the many forms of intensive treatment which have been tried in different clinics in the U S A are reviewed below.

Recently the United States Public Health Service (1944) published an analysis of the results of 4,351 intensive treatments practised in twenty-two clinics.

The methods employed were rapid intravenous drip, the daily dose of mapharsen (0.18 gm.) being given in an hour on each of the five days, multiple injections at the rate of two of 0.06 to 0.1 gm. a day for five to ten days, multiple injections of mapharsen, totalling 0.6 to 0.9 gm., in conjunction with two days of fever in a course lasting ten days, and multiple injections of arsphenamine at the rate of four a day for six days. The analysis

was directed by the Principal Statistician of the U S Public Health Department, and the main results were as follows—Of the cases treated, 3,575 are reported to have been followed sufficiently after treatment to enable a result to be recorded, and those classed as having achieved a satisfactory result had been negative for at least three months at the time of the evaluation—not a very high standard. On this basis, the satisfactory results of the six series were 85·7 per cent. of the primary cases and 70·4 per cent. of the secondary. The best results were with neosphenamine (89·5 per cent in primary cases and 85·7 per cent in secondary), in the mapharsen series the best results were in 637 cases treated with this remedy in conjunction with fever induced by typhoid vaccine, 88·5 per cent of the primary cases and 70·4 per cent. of the secondary cases so treated being regarded as satisfactory.

It is mentioned in the report that in a portion of the cases bismuth was also given and, without giving the actual numbers of cases so treated, the authors estimate that in the rapid drip series the satisfactory results were 70·4 per cent of those receiving mapharsen alone but 92·4 per cent of those receiving bismuth concurrently. In the slow drip series there was no significant difference between those receiving mapharsen and bismuth and those treated with mapharsen alone.

An interesting outcome of the analysis was the discovery that in each series the proportion of satisfactory results was higher in those aged twenty-five years and over than in younger patients. Also, that whites responded to the treatment better than did coloured patients and males better than females. Encephalopathy occurred in 7·1 per 1000 of those treated (3·2 fatal), no difference in respect of this complication was discovered in the different methods.

Pillsbury *et al* (1944) have reported on the results of a treatment in which 1 mgm mapharsen per kgm body weight was given each day for twenty days and during the same period eight injections of bismuth salicylate (0·2 gm in each). The total number treated was over 3,000, all but two being men of the U S Army. There was no death, but toxic reactions were frequent and freedom from disaster was attributable in no small degree to skilled supervision in hospital. Of 204 sero-negative primary cases observed for four months or longer, all remained negative, of 169 sero-positive primary cases, 7 were positive when last tested, and of 61 secondary cases, 6 were positive (4 at four months and 2 at six months). The method of treatment described was clearly one only for selected patients under skilled supervision in hospital.

Important modifications of the treatments outlined above have resulted from animal experiments conducted by Eagle and Hogan (1942, 1943). These workers sought to discover a reasonable compromise between the dangerous five-day treatment and the tedious but relatively safe one lasting sixty-nine weeks which has already been mentioned. As a result of their experiments they concluded that the curative dose of mapharsen for animals was the same whether it was administered by one injection or by many over a period of eight weeks. On the other hand, the mortality was inversely proportional to the length of time over which the treatment was spread.

Recently, Eagle (1944) has reported on the results of schemes of treatment based on the above experimental work, which were tried out in eighty-six clinics on 4,823 patients, of whom 3,394 had primary or secondary syphilis. In the schemes described in Eagle's article three injections a week of 1 mgm. mapharsen per kgm. (with a maximum of 80 mgm. and a minimum of 40 mgm.) were given for periods ranging from four to twelve weeks, the numbers of injections ranging from less than nine to more than twenty-seven, but nearly three-quarters receiving more than twenty injections. In two-thirds of the cases bismuth was given concurrently at the rate of 0·2 gm. of the subsalicylate per week. The results in cases treated

without bismuth are described as having been "uniformly poor regardless of dosage." Those with bismuth are described as follows —

"Tri-weekly injections of mapharsen with weekly injections of bismuth proved highly effective. In patients receiving an average total of 1,600 mgm. (21 mgm. per kgm. or more) plus an average total of nine injections of bismuth, the cumulative percentage of treatment failures was 9.3, and the cumulative percentage of 'cures' fifty to sixty weeks after the beginning of treatment was 82. A decrease in either mapharsen or bismuth to less than these amounts resulted in a higher proportion of treatment failures."

Serious toxic reactions occurred in 39 cases of the series, they included toxic encephalopathy (1 fatal), 3 blood dyscrasias, 7 dermatitis, 4 nephritis (2 fatal) and 21 jaundice (1 fatal).

Readers may reasonably wonder what advantage this course of treatment, which lasted nine to twelve weeks, offers over one in which 5-8 gm. neoarsphenamine and 2.0 to 2.4 gm. bismuth metal are given in nine weeks with less inconvenience and danger to the patient. It is true that the neoarsphenamine-bismuth course has not been evaluated so elaborately as has that instituted by Eagle, but Gennerich's results provide guidance as to its possibilities, and neither it nor the Eagle course is sufficient for recommendation to the patient who rightly asks that everything that is reasonably possible shall be done to insure against relapse. Fortunately, there is now another therapeutic agent, penicillin, with the help of which it may reasonably be hoped to reduce considerably the duration of anti-syphilitic treatment.

PENICILLIN—Since the first report by Mahoney, Arnold and Harris (1944) on the treatment of four cases of early syphilis with penicillin, there has been a spate of articles on the same subject, and only a few of those which give some guidance in the use of the remedy in syphilis can be reviewed here. Mahoney and his colleagues (1944) later published a report on 100 cases treated each with 20,000 units given intramuscularly every three hours for sixty doses.

Of the 100 cases, 52 had been observed for an average of 135 days. Of 30 primary cases in the group, 25 had remained well for 75 days or longer; three had relapsed after 64, 112 days, and nine months, respectively, and two were becoming negative at the time of reporting. Of 22 secondary cases, 11 had become and remained negative, and in the other there was a probability of failure.

Moore *et al.*, members of the Penicillin Panel of the Sub-committee on Venereal Diseases of the National Research Council, U.S.A. (1944), reported on 1,418 early cases of syphilis treated with penicillin in twenty-three clinics, with doses ranging from 60,000 to 1,200,000 units.

In two of the series the patients also received 320 mgm. mapharsen at the rate of 40 mgm. a day, with considerably better effects than in patients receiving penicillin alone. Thus, whereas 60,000 units of penicillin was followed by 13 relapses in 46 cases, the same dose in conjunction with mapharsen was followed by no relapse in 26 cases. Similarly, in 138 cases treated each with 300,000 units there were 14 relapses, but in 68 treated with the same dose in conjunction with mapharsen there were only 4 relapses. After administration of 1,200,000 units there were 4 relapses in 191 cases.

In 20 infants with congenital syphilis, who were treated with 20,000 units per kgm., the response was similar to that in acquired syphilis. The authors reported that in respect of disappearance of spirochaetes and healing of lesions the effect of penicillin seemed to be similar to that of the arsphenamine preparations. The period of observation of the patient after completion of the penicillin treatment was, however, much too short to permit of final conclusions being drawn, and it is probable that with longer observation more relapses would have been found.

The impression derived from this report, as indeed from all similar reports, is that reliance on penicillin alone would be a mistake. On the other hand, the results suggest that a course of treatment with penicillin concurrently with some arsenic

and bismuth would be equivalent to much arsenical and bismuth treatment, and on this basis directors of civilian treatment centres have recently been recommended to give as routine to early cases of syphilis the following treatment —

(a) During $7\frac{1}{2}$ days, 2,400,000 units of penicillin at the rate of 30,000 every three hours, two doses of 0.45 gm. neoarsphenamine and an injection of a bismuth compound containing 0.2 to 0.24 gm. bismuth metal, and (b) a course of 10 injections of neoarsphenamine concurrently with 10 of bismuth, such as was outlined earlier in this article. It is suggested that if it is not convenient to start the penicillin-arsenic-bismuth course at the time the diagnosis is made, the ordinary neoarsphenamine and bismuth course should be started and the penicillin course be interpolated in it or follow immediately after it. If the penicillin course is postponed still further, the arsenical and bismuth treatment should proceed as in pre-penicillin days, but as soon after that as the $7\frac{1}{2}$ day course of penicillin, arsenic and bismuth has been given the treatment should be suspended, the patient being placed under observation with blood tests, and so forth.

In this scheme the arsenical remedy recommended is neoarsphenamine. I have studied carefully all the available evidence I could obtain on the respective merits of neoarsphenamine and preparations of the arsenoxide class, and I do not believe that the slogan "less toxic and more efficient" often applied to the latter is justified.

It will be appreciated that a satisfactory method of slowing the rate of absorption and excretion of penicillin, such as that of Romansky and Rittman (1944) already mentioned, would reduce the number of injections required for administration of the recommended 2,400,000 units and would thus be of immense practical value. In this connexion, attention is due to the work of Lloyd Jones and Maitland (1945b), who found that after a single intravenous injection of 300,000 units, penicillin could be detected in the urine for seventeen hours, and after 500,000 units for twenty-eight hours. After a single intramuscular injection of 300,000 units, penicillin was found in the urine for twenty-three hours. On this basis they treated 65 cases, each with a single daily dose of from 300,000 to 500,000 units given intravenously, and two with a single daily dose given by the intramuscular route, the total dose ranged from 1,200,000 to 500,000 units. The results seem to have been promising, but such a method is not recommended for the treatment of civilian cases of syphilis until it has been well tried out in such a disease as gonorrhœa, in which results are more quickly decided.

On the use of penicillin in late syphilis, a valuable preliminary report by Stokes *et al* (1944) ends thus —

"As a general statement of the situation in a single sentence, we may say that penicillin, as sodium salt of an as yet incompletely analysed and understood substance, is an effective therapeutic agent in the treatment of late syphilis. Under conditions not yet clearly defined, it produces transformations symptomatically and serologically without reaction, or even serious inconvenience to the patient, which are equal, if not superior, to those obtained by long and arduous procedures involving the arsenicals and heavy metals."

The details of cases reported in the article show most encouraging, and even brilliant, results in such unpromising material as general paresis and tabo-paresis.

In tabes and general paresis good results have been reported by Goldman (1945) after intra-thecal injections of penicillin.

The dosage was 10,000 units (in 2 c.cm.) on each of two successive days and 20,000 (in 4 c.cm.) on each of four more days. A 20 c.cm. syringe containing the dose was attached to the lumbar puncture needle and filled up with spinal fluid. The syringe was then detached and the contents thoroughly mixed, after which the syringe was again attached to the lumbar puncture needle and the contents slowly emptied into the spinal canal, this portion of the operation taking five minutes.

In tabes, the effect on severe lightning pains seems to have been excellent after all other methods had failed

In the prevention of congenital syphilis by treating pregnant women, Lentz *et al* (1944) have reported encouraging results. In six women with early syphilis who were treated with 1,200,000 units the infant was born apparently healthy

CONCLUSION

Altogether, although still far from knowing the possibilities and limitations of penicillin in the treatment of both gonorrhœa and syphilis, there are clearly grounds for sober optimism, and it does not seem too much to hope that with the present resources for dealing with these two diseases, they may quickly become a minor public health problem

References

- Barritt, M M (1943) *Brit med J*, **1**, 254
 — (1944) *Ibid*, **1**, 494
 Beattie, J, and Marshall, J (1944) *Ibid*, **1**, 547
 Bigger, J W (1943) *Lancet*, **1**, 457
 Culp, O S, Magid, M A, and Kaplan, J W (1944) *J Urol*, **51**, 655
 Eagle, H (1944) *J Amer med Ass*, **126**, 538
 —, and Hogan, R B (1942) *Science*, **95**, 362
 —, — (1943) *Vener Dis Inform*, **24**, 33, 69, 159
 Gennerich, W (1914) *Münch med Wschr*, **61**, 113
 Goldman, D (1945) *J Amer med Ass*, **128**, 274
 Greenblatt, R B, *et al* (1943) *Amer J Syph*, **27**, 30
 Haber, H (1945) *Brit J Vener Dis*, **21**, 63
 Harrison, L W (1931) *The Practitioner*, **126**, 193
 — (1935) *Brit J Vener Dis*, **11**, 69
 —, and Osmond, T E (1943) *Ibid*, **19**, 108
 Hyman, H T, Chargin, L, and Leifer, W (1939) *Amer J Syph*, **23**, 685
 Jones, T R L, Martland, F G, and Allen, S J (1945a) *Lancet*, **1**, 368
 —, — (1945b) *Brit J Vener Dis*, **21**, 65
 Jones, M (1942) *US Nav med Bull*, **40**, 113
 Klue, E F, and Ryan, T C (1942) *US Nav med Bull*, **40**, 360
 Leifer, W, Chargin, L, and Hyman, H T (1941) *J Amer med Ass*, **117**, 1154
 Lentz, J W, *et al* (1944) *Ibid*, **126**, 408
 Loveless, J A, and Denton, W (1943) *Ibid*, **121**, 827
 MacCallum, F O (1943) *Brit J Vener Dis*, **19**, 62
 Macgregor, J V (1945) *Brit med J*, **1**, 593
 Madsen, Th (1924) *Hlth Org L O N C 5 M 5*, 1924 (CH 148), p 116
 Mahoney, J F, Arnold, R C, and Harris, A (1943) *Amer J Pub Hlth*, **33**, 1387
 — *et al* (1944) *J Amer med Ass*, **126**, 63
 Martenstein, H (1935) *Quart Bull Hlth Org, L O N*, **4**, 129
 Milinska, Sophie (1924) (see Madsen, p 95)
 Moore, J E, *et al* (1944) *J Amer med Ass*, **126**, 67
 Osmond, T E (1945) *Brit med J*, **1**, 853
 Pillsbury, D M, *et al* (1944) *Brit J Vener Dis*, **20**, 154
 Ransome, G A, Paterson, J C S, and Gupta, G M (1945) *Brit med J*, **1**, 659
 Romansky, M J, and Ruttman, G E (1944) *Science*, **100**, 196, *Bull US Army med Dep*, No 81, p 43
 —, Murphy, R J, and Ruttman, G E (1945) *J Amer med Ass*, **128**, 404
 Salaman, M H, *et al* (1944) *Lancet*, **2**, 7
 Shafer, Bertha, and Zakon, S J (1944) *Arch Derm Syph N Y*, **50**, 200
 Sheehan, H L (1944) *Lancet*, **2**, 8
 Sorsby, A (1945) *Brit med J*, **1**, 903
 Stokes, J H, *et al* (1944) *J Amer med Ass*, **126**, 73
 United States Public Health Service (1944) *Ibid*, **126**, 554
 Van Horn, E C, and Dakin, T R (1944) *Vener Dis Inform*, **25**, 365
 Zinnamon, B L, and Seeberg, V P. (1945) *Ibid*, **26**, 31

PULMONARY TUBERCULOSIS

By L E HOUGHTON, M D

Physician to the Middlesex County Council Tuberculosis Service, and to the County Hospital, Harefield

[T was frequently stated by experienced clinicians in the past that early diagnosis of pulmonary tuberculosis carried with it a graver prognosis than diagnosis made at a more advanced stage of the disease. This apparently cynical observation was made before the days of routine X-ray diagnosis, when a minimal lesion which declared itself by severe symptoms was probably less amenable to conservative treatment than the more insidious and less incapacitating infiltrations which often developed undetected. For these same reasons a patient with a localized lesion recognized as the result of hæmoptysis was considered to be fortunate. The reversal of these opinions in modern clinical thought provides a measure of the advances which have been made, both in diagnosis and in the control of established disease. The old concept that "you must have a cavity before you are cured," has lost much of its validity, and the chief preoccupation of phthisiologists at the present time is the elimination of intra-pulmonary cavities. Most recent advances in treatment have been directed towards this end.

ETIOLOGY

There has been a good deal of modification of the belief that the prime factor in the etiology of tuberculosis is fortuitous infection by Koch's bacillus. The specific organism is perhaps a detonator which initiates a violent reaction in a vulnerable individual, and the rôle of genetic, temperamental and environmental factors in producing gross tissue reactivity is receiving more attention from clinicians. The effect of anxiety and abnormal stress is probably as potent a cause of increased morbidity in war time as the effect of malnutrition, and certainly these influences are more significant than closer contact with a more virulent organism under war conditions.

It is now recognized that, although infection by Koch's bacillus is almost inevitable in civilized communities, the infection does not necessarily occur in childhood, but under improved hygienic conditions is tending to be postponed into early adult life, or even later, in an increasing proportion of the population. It should be noted that a negative Mantoux reaction does not necessarily preclude previous infection, for the hypersensitive reaction may disappear in a small proportion of individuals (Rich, 1944).

The primary complex (localized focus of infection in lung parenchyma or elsewhere, with involvement of corresponding lymph glands) is diagnosed with increasing frequency, and its dissociation from progressive disease in the great majority of cases is now well established. The transitory lesions of primary infection are not always easy to distinguish radiologically from the early infiltrations of

pulmonary tuberculosis (progressive bronchogenic tuberculosis), particularly when they occur in adults, and symptoms when they arise may be indistinguishable from influenza or any other mild febrile disturbance. These primary phenomena have been extensively studied in nurses in this country (Daniels, 1944, Edwards, Penman and Blair, 1945) and in Scandinavia (Heimbeck, 1936, Scheel, 1935). Ustvedt (1942) considers that progressive lesions when they occur are apt to follow closely upon primary infection. Phenomena associated with the primary or early post-primary phases are pleurisy, erythema nodosum and phlyctenular conjunctivitis. It is possible that the clinical separation of the phenomena of primary tuberculous infection from progressive and established tuberculous disease will lead to a modification in the existing notification procedure.

Work of great interest on the genetic factors in the etiology of tuberculous disease has recently been carried out in the United States (Kallman and Reisner, 1943). The investigation covered 308 twin pairs with manifest (adult type) pulmonary tuberculosis, together with an unselected sample of relatives comprising 930 full brothers and sisters, 74 half-siblings, 688 parents and 226 marriage partners. The adjusted mortality rates for the groups were as follows—For the general population of the State and City of New York the rate was 1.4 per cent., for the husbands and wives (of tuberculous twins) 7.1 per cent., for their half-sibs 11.9 per cent., for their parents 16.9 per cent., for their full sibs 25.5 per cent., for their fraternal co-twins 25.6 per cent., for their identical co-twins 87.3 per cent.

The high husband and wife figure is partly accounted for by the selective factor. In spite of the intimate contact of husband and wife, however, the rate even for half-sibs is much higher. It will be noted that identical co-twins are three-and-a-half times more likely to be affected than fraternal co-twins. Even more striking is the course taken by the disease in affected cases, illustrating as it does the importance of the genetic factor in resistance to established disease. When resistance is poor in one identical twin it is almost certain to be poor in the other, whereas the chances of death from pulmonary tuberculosis of a person with the disease who has a healthy identical twin are practically nil. In a commentary on this work (*Brit med J*, 1944, 2, 504) it is stated that "if it is not possible to segregate a tuberculosis case in a hospital it is at least advisable not to have the nearest relatives of the patient take care of him. Nurses who undertake tuberculosis nursing should be selected if possible as being free from tuberculosis histories in their families."

DIAGNOSIS

The introduction of mass miniature radiography has raised the hope that ultimately infection may be controlled by the weeding out from the population of unsuspected cases of open tuberculosis. By the routine X-ray survey of the whole population it is hoped to discover (1) the early case, (2) the unsuspected chronic case, and (3) non-tuberculous chest conditions. The scheme is still largely in an experimental stage, but results of considerable interest have already been achieved. The average pick-up of tuberculosis cases requiring treatment among the civilian population is 3 to 4 per 1000 (*Med Res Coun Rpt*, 1945).

Critics of the scheme have called attention to the vast expenditure of effort and money for a small yield, to the difficulty in providing treatment for cases so discovered, and to the possible induction of a sense of false security or, alternatively, of neurosis among sections of the population. Discussion of the application of the method centres around the desirability of surveying the whole population indiscriminately or concentrating upon selected groups, such as those presenting symptoms (Toussaint and Pritchard, 1944). Believing that pulmonary tuberculosis is seldom completely symptomless, I favour the latter approach.

The wider application of sputum-culture methods constitutes an advance, both in diagnosis and in the management of the established case. The gastric lavage technique is still the method of choice in children, who usually swallow their sputum, but the laryngeal swab method (Nassau, 1941) combines simplicity with a high standard of reliability.

TREATMENT

CHEMOTHERAPY—No effective chemotherapeutic agent has yet been demonstrated for tuberculosis. A number of compounds have been shown to inhibit the growth of tubercle bacilli *in vitro*, and one compound, promun or promanide, is said to arrest, but not completely suppress, the disease in guinea-pigs (Hinshaw and Feldman, 1941). It was found to be ineffective and toxic when tested in human tuberculosis, but it has been claimed that it has some value when applied to local ulcerations (Tytler and Lapp, 1942). Penicillin is apparently ineffective *in vitro* and *in vivo* against the tubercle bacillus. Salts of heavy metals, such as sanocrysin and barium salts, are effective in animal experiment, but after prolonged trial in the human subject they have been largely abandoned for clinical use.

Tuberculous empyema—Chemotherapy has proved of considerable value in the management of tuberculous empyema. Azochloramid, together with a "wetting agent" (sodium tetradecyl sulphate), is often effective in diminishing the formation of pus, rendering it thinner and even, in some cases, sterile (Petroff, 1941, Ashman and Tate, 1943).

When a tuberculous empyema becomes secondarily infected, the sulphonamides and penicillin have proved of the utmost value in sterilizing the pleural fluid and so retrieving cases which would previously have been regarded as almost hopeless. Penicillin should always be used prophylactically in spontaneous pneumothorax of tuberculous origin to prevent secondary infection.

COLLAPSE THERAPY

The scope of this article does not permit a detailed account of the indications for each of the surgical manœuvres which are so prominent in the strategy of the tuberculosis physician. No case is specifically suitable for any one approach, but all manœuvres can be brought to bear in order to achieve the best mechanical result. The advances which have been made in collapse therapy during the past fifteen years have resulted from methods of trial and error, with the gradual development of a painfully acquired, but more rational technique (see fig 1-7).

ARTIFICIAL PNEUMOTHORAX—It has been estimated (Block, Tucker and

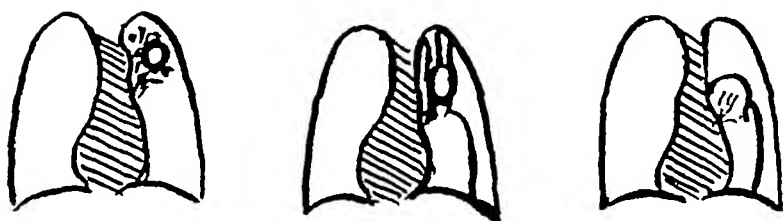


FIG 1—Successful artificial pneumothorax and adhesion section



FIG 2—Acute exudative lesion treated by pneumothorax without previous bed rest. Massive atelectasis with patent cavity, followed by tuberculous empyema and contralateral spread

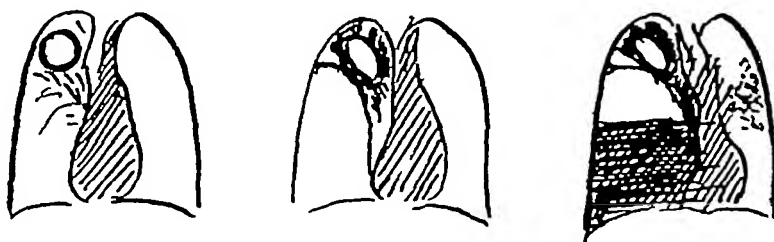


FIG 3—Contra-selective pneumothorax with totally adherent apex, followed by tuberculous effusion and contralateral spread

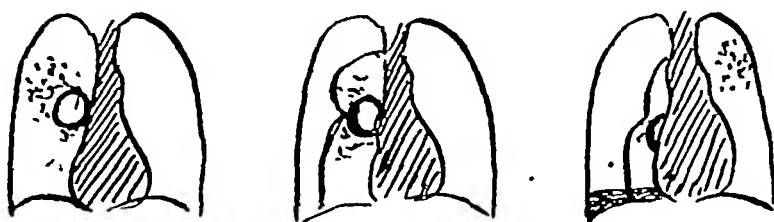


FIG 4.—Large cavity in apex of lower lobe. Pneumothorax fails to close cavity, which disappears behind the heart shadow

PULMONARY TUBERCULOSIS

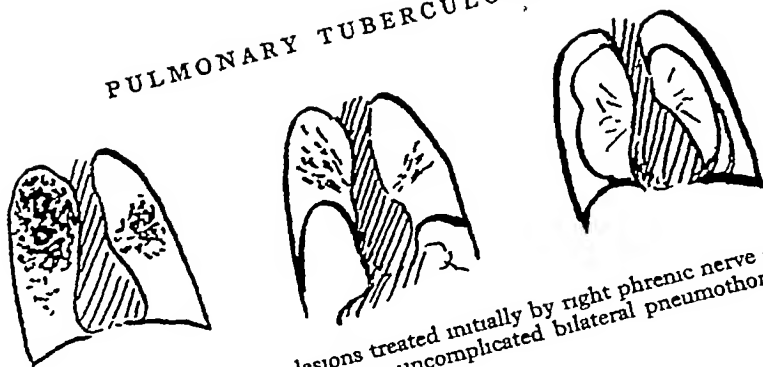


FIG 5—Bilateral acute exudative lesions treated initially by right phrenic nerve crush and pneumoperitoneum, followed later by uncomplicated bilateral pneumothorax

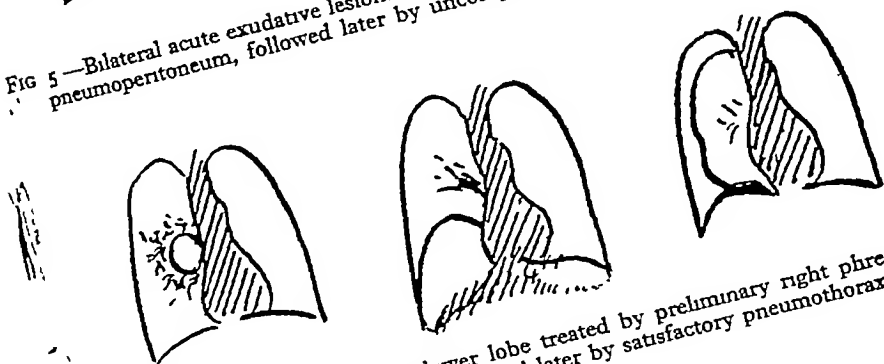


FIG 6—Large cavity in apex of lower lobe treated by preliminary right phrenic nerve crush and pneumoperitoneum, followed later by satisfactory pneumothorax.

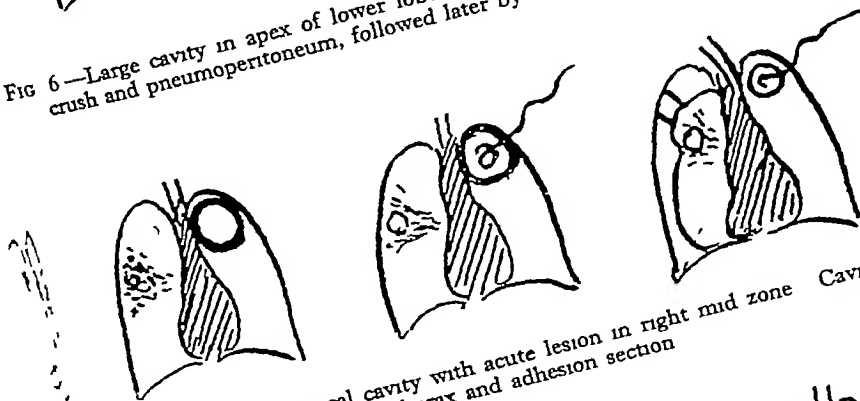


FIG 7a—Very large apical cavity with acute lesion in right mid zone followed by right pneumothorax and adhesion section Cavity drainage

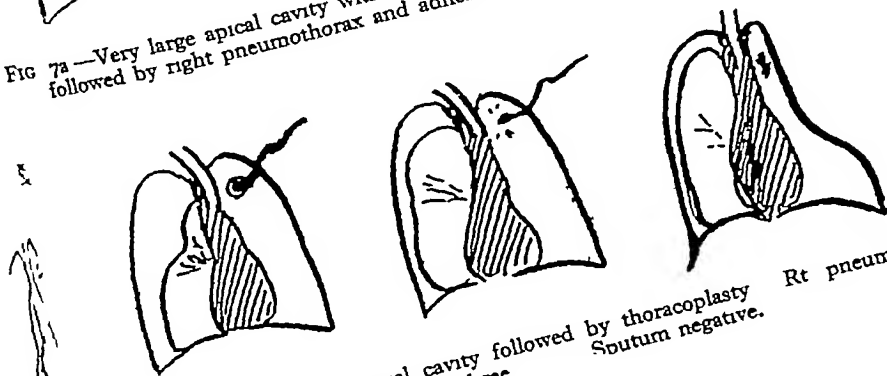


FIG 7b—Closure of left apical cavity followed by thoracoplasty Sputum negative. Rt pneumothorax maintained Patient at work for three

Adams, 1941) that approximately 2,100 articles on pneumothorax appeared during the 1929-1939 decade but that only 4.7 per cent of these dealt with results of treatment. The same authors present a review of the sounder papers dealing with the effects of treatment, and, in emphasizing the wide variations in results claimed, they point out that the standards adopted by many writers were quite inadequate. It must also be realized that the type of collapse therapy now being applied has little in common with pneumothorax as it was used in the 1920's and early 1930's. Rafferty (1944) concludes that "despite its value, pneumothorax is far from being a panacea and must be regarded as nothing more than an effective aid in the total therapy of tuberculosis."

The main object of the surgical devices, including pneumothorax, which are employed is the closure of cavities and the consequent prevention of relapse. That collapse or relaxation of the affected lung has also an empirical effect on progressive lesions is undoubted in certain cases, but the area of disease must not be so great, or the condition so acute, as to involve the risk of massive atelectasis. This latter complication is a most serious one in any form of collapse therapy and it is the precursor of empyema, bronchiectasis and unexpandable lung; it also favours persistent cavitation and subsequent spread of disease. Massive atelectasis of lung or lobe must be avoided as rigidly as contra-selective collapse with adhesions, for it is these two complications which substantially account for the disappointing end-results of artificial pneumothorax treatment which are reported in so many quarters. Artificial pneumothorax in inexperienced hands is a most dangerous procedure. This is particularly so as the early effect is often pleasing to all concerned, and the disastrous nature of the step which has been taken only becomes clear many months later when the initial mistake has been forgotten. Artificial pneumothorax should seldom or never be induced without adequate preliminary bed rest, without access to all the surgical facilities which may subsequently be required, and without a considerable experience in the management of such patients from the surgical, medical and psychological points of view.

Apart from the timely reversion to the belief that treatment of the patient is as important in prognosis as the treatment of the cavity, the most significant recent development in the management of pulmonary tuberculosis is the appreciation of the rôle of the bronchus, both in the pathology of the condition and in the response to collapse therapy.

Tuberculous endo-bronchitis (tracheo-bronchitis)—Although it is customary to regard pulmonary tuberculosis as essentially a condition involving destruction of the lung parenchyma, it is probable that this process is secondary to, and is conditioned by, changes in the bronchi. This is probably true also of other, non-tuberculous, inflammatory processes in the lung. The initial change is an exudative process in the bronchioles, involving œdema of the bronchial mucosa (probably an allergic manifestation) which, together with the extrusion of mucoid material, leads to the blockage of the bronchial lumen. The result is a small area of atelectasis which appears on the X-ray as an area of "infiltration." If the area is sterile, the ultimate result may be fibrosis, if it is infected, the result will be local suppuration and perhaps abscess formation or, in the case of tuberculous infection, caseation and perhaps cavity formation. In any case the bronchi tend to become

bronchiectatic and distorted. These phenomena can be readily demonstrated by bronchography (Dormer, Friedlander and Wiles, 1945). In progressive and extensive pulmonary tuberculosis the larger bronchi become involved, and this leads not only to widespread bronchiectasis, but also to localized narrowing due to edema and ulceration, and distortion of the bronchial tubes. The result is frequently the development of a one-way check valve, so that air can pass into the bronchus on inspiration but is checked and retained on expiration. This is the mechanism responsible for the appearance of *distension cavities* in the lung, which constitute one of the major problems facing the collapse therapist.

CONTRAINDICATIONS TO PNEUMOTHORAX—From the considerations briefly outlined above, certain contraindications to pneumothorax emerge which can be tabulated as follows—

- (1) *Primary lesions*—because a main bronchus may be stenosed by glandular pressure and this may lead to atelectasis and unexpandable lung. The condition is best left alone, because the course is usually benign.
- (2) *Tuberculous ulceration* of a main bronchus with narrowing of the bronchial lumen—for the same reasons as in (1). Thoracoplasty is the procedure of choice if the parenchymal lesion is sufficiently localized to warrant interference. The risk of bronchial occlusion and atelectasis is not so great with this procedure.
- (3) *Acute exudative lesions*—because the smaller bronchi are œdematous and partially occluded by viscid mucus. Pneumothorax causes complete bronchial occlusion, atelectasis with retained secretions followed by tuberculous empyema. A period of bed rest, perhaps combined with phrenic nerve crush, and/or pneumoperitoneum (see p. 240) is essential as a preliminary to pneumothorax.
- (4) *Large apical or dorsal lobe cavities*—because the draining bronchi tend to become further distorted during pneumothorax, with increase in the efficiency of the check-valve mechanism. Thoracoplasty, combined with cavity drainage (see p. 240) is indicated.

INDICATIONS FOR PNEUMOTHORAX—An understanding of the limitations and potential dangers of pneumothorax treatment does not detract from its value in suitable cases. On the contrary, it can be attempted with more confidence, and if danger arises the pneumothorax can be readily abandoned in favour of some other form of treatment. Apart from the contraindications which are mentioned above, there are few cases which come under review in which pneumothorax is not seriously considered sooner or later. Perhaps the greatest difficulty arises, on the one hand, in the case with a minimal lesion and, on the other hand, in the case with extensive bilateral lesions.

The minimal lesion—With the improvement of methods of diagnosis, and particularly as the result of mass X-ray surveys, minimal lesions are being brought to light with increasing frequency. Perhaps a small shadow in one lung is seen on X-ray, which is not more than a centimetre or two in diameter and which is believed to be tuberculous in origin, but which shows no sign of clinical activity. In some cases this may be the beginning of serious trouble and in others it may be without

clinical significance. Such cases present considerable difficulty, and some authorities favour the induction of pneumothorax as a prophylactic measure. This involves, however, hospitalization and notification, which in many cases would seem to be a drastic and unjustifiable step.

Undoubtedly the best procedure to follow is close clinical observation for a period of not less than two years. For the first six months an X-ray should be taken every six weeks and thereafter every three months. If the lesion shows any sign of extension or breaking down into a small cavity, pneumothorax should be induced without further delay. Laryngeal swab or gastric lavage culture should also be carried out at regular intervals, but it is probable that a single positive result should not be regarded as decisive. The development of symptoms, cough or loss of weight and energy, would call for immediate review of the case. The sedimentation rate is an unreliable index of activity, but a steadily increasing rate would have some significance.

Extensive lesion—If lung destruction is so extensive that the patient has little or no respiratory reserve, collapse therapy is obviously not feasible. But within certain limits a good deal of salvage work can be attempted if the patient has at length brought his lesions under temporary control. Bilateral pneumothorax, if carefully managed, is frequently most successful. It is becoming increasingly common, moreover, to use pneumothorax to control the less affected lung while thoracoplasty is being undertaken on the other side. Combinations of phrenic nerve crush and pneumothorax or thoracoplasty may form part of the programme of treatment. Many recent advances in the surgery of pulmonary tuberculosis, such as the combination of cavity drainage and thoracoplasty, are effective in the advanced case. It is misleading to state that the early case is necessarily the most amenable to curative treatment (see page 233).

Duration of pneumothorax—No rules can be laid down for the length of time that a successful pneumothorax should be maintained. It depends entirely upon the extent and type of the original lesion, and upon the individual patient. If the original lesion was minimal, perhaps two years' treatment would suffice, if an extensively damaged lung has been brought under control the pneumothorax should probably be maintained indefinitely.

CAVITY DRAINAGE

A fine catheter is introduced into the cavity by means of a trocar and canula passed through the chest wall (Monaldi, 1939). The pleura must be adherent at the site of introduction. Continuous suction is applied to the cavity by means of a small electric pump, and in a high proportion of cases reduction in the size of the cavity or complete temporary closure can be achieved. Subsequent thoracoplasty need then be only minimal in extent. A recent advance in surgical technique is *anterior stage thoracoplasty*. The first and second ribs are removed from the front before the introduction of the Monaldi tube. This obviates the risk of infecting the wound from the tube drainage track when thoracoplasty takes place after cavity drainage.

Dorsal lobe cavities can often be closed by a combination of phrenic nerve paralysis and *pneumoperitoneum*. The latter procedure consists in introducing air

into the peritoneal cavity with a view to raising the diaphragm and so relaxing the lung. Refills of 1000 c cm to 1500 c cm are given weekly. The procedure is not without complications but is often effective in augmenting the diaphragmatic rise obtained by phrenic nerve interruption. It is not only effective for dorsal lobe cavities, but is used as an ancillary treatment for various types of lesion and in various phases of the disease.

SOCIOLOGICAL CONSIDERATIONS

Reference should be made to the government scheme of allowances for tuberculous persons which has been introduced during the war (Memorandum 266/T). Designed primarily as a war measure to facilitate the return of diagnosed cases to industry, this scheme is an advance, not only in social medicine, but as a material aid to treatment. By assisting the patient and his dependants during this crisis in his affairs, the patient is not only relieved of anxiety but is more easily reconciled to the prospect of prolonged institutional treatment. At present the allowances are only available to those patients who have a prospect of returning to industry within a reasonable time, and the more chronic cases are excluded from benefit. This is a source of dissatisfaction and hardship. The war has added a measure of urgency to the old crusade for rehabilitation of the tuberculous, but the problem remains unsolved. Tuberculosis is not a static disability. When it becomes static it is no longer a disability. The colonies continue to command a measure of support from practitioners and patients, but the latter cannot be said to be enthusiastic supporters of the scheme.

Specific preventive measures have as yet recorded no progress, and B C G vaccine still awaits an extensive trial in this country. The mitigation of "want" and "fear" may in the future accelerate the recently interrupted downward trend of tuberculosis mortality rates.

References

- Ashman, D. Munro, and Tate, M. G. (1943) *Tubercle*, 24, 181.
 Block, R. G., Tucker, W. B., and Adams, W. E. (1941) *J thorac Surg*, 10, 310.
 Daniels, M. (1944) *Lancet*, 2, 165, 201, 244.
 Dornier, B. A., Friedlander, J., and Wiles, F. J. (1945) *Amer Rev Tuberc*, 51, 455.
 Edwards, P., Penman, A. C., and Blair, L. G. (1945) *Lancet*, 1, 429.
 Fowler, W. O. (1941) *Trans nat Tuberc Ass*, 37, 142.
 Heimbeck, J. (1936) *Tubercle*, 18, 97.
 Hunshaw, H. C., and Feldman, W. H. (1941) *J Amer med Ass*, 117, 1066.
 Jones, C., and Macdonald, M. (1943) *Tubercle*, 24, 97.
 Kallman, F. J., and Reisner, D. (1943) *Amer Rev Tuberc*, 47, 549.
 Monaldi, V. (1939) *Sett Med*, 27, 231.
 Nassau, E. (1941) *Proc roy Soc Med*, 34, 397.
 Petroff, S. A. (1941) *Amer Rev Tuberc*, 44, 738.
 Rafferty, T. N. (1944) "Artificial Pneumothorax in Pulmonary Tuberculosis," London.
 Rich, A. R. (1944) "The Pathogenesis of Pulmonary Tuberculosis," Baltimore.
 Scheel, O. (1935) *Nord med Tidsskr*, 9, 481.
 Toussaint, C. H. C., and Pritchard, E. K. (1944) *Postgrad med J*, 10, 143.
 Tytler, W. H., and Lapp, A. D. (1942) *Brit med J*, 2, 748.
 Ustvedt, H. J. (1942) "Pulmonary Tuberculosis and Its Treatment," London.

CHILD HEALTH

XVI—THE CARE OF THE CRIPPLED CHILD

By M FORRESTER-BROWN, M D, M S

Senior Surgeon, Bath and Wessex Orthopædic Hospital

THE care of the crippled child was the subject of a great campaign by Sir Robert Jones and his pupils after the first world war, when they pleaded that the method which had so largely prevented crippling in wounded soldiers should be available for the prevention and treatment of crippling in children. The campaign resulted in the establishing of central hospitals and a ring of out-patient clinics based on them in such well-known centres as the Robert Jones and Agnes Hunt Hospital, Oswestry, the Woodlands, Birmingham, the Wingfield-Morris, Oxford, the Bath and Wessex, Bath, the Princess Elizabeth, Exeter, and many others, forming a network over the whole of Britain, into whose meshes have been gathered thousands of cripples and potential cripples. Indeed, so great has been the success of this system that at the outbreak of the present war the title of this article was almost an obsolete term. The war, however, which has played havoc with so many of the fruits of civilization, has not spared the orthopædic schemes, many of which have been partly disintegrated, some having lost their surgeons to war service, others their buildings, skilled nursing-staffs, and so on, whilst the mass movements of population in evacuation have broken the continuity of treatment, which is so essential for success in these cases. Fortunately, every effort was made to keep patients after evacuation under the local scheme of the area into which they moved, and this must have prevented a great deal of otherwise unavoidable crippling.

The arrival of peace in Europe has not put the position back to normal, for the aftermath of scarcity of hospital beds, of nursing and domestic personnel, both skilled and unskilled, and of fully trained orthopædic surgeons, makes it difficult to carry on the schemes which survived the hostilities, let alone to expand them or open new ones. It is to be hoped that the plans of the new government for expanding hospital accommodation will not be based on bricks and mortar alone, without due consideration for the fact that a skilled staff can produce results under the most primitive conditions—witness Dame Agnes Hunt's pioneer work in her original manor house, and lately the fine surgery based on operation trucks in the desert—conversely, the ideal building achieves nothing when run by a staff inadequate in numbers, or in experience. At the present moment, hundreds of empty beds are available in the military hospitals recently vacated by U.S.A. medical staff, yet hardly any existing hospital can utilize a single one of their wards for lack of personnel of every type.

THE MAIN CAUSES OF CRIPPLING

Measures cannot be planned for the treatment of crippling, let alone its prevention, unless the primary or secondary causes of the evil are appreciated. At the time of

Sir Robert Jones's initial campaign these were of four main groups rickets, tuberculosis of bones and joints, poliomyelitis, and congenital defects. These will now be considered in more detail.

Rickets as a cause of severe bony deformity has been practically abolished by the infant welfare schemes and the education of the public in the importance of vitamins. Mild degrees of rickety bone changes are still found in children, both breast fed and dosed continuously with vitamins, and the cause of this is a subject for research by the physicians.

Tuberculosis of the bones and joints was tending to diminish in incidence, when all the unfavourable conditions of life in war time, particularly black-out, housing shortage and food scarcity, gave it the chance to increase. It is not always remembered that an increase in pulmonary tuberculosis also spreads the opportunities for young infants and school children to acquire the infection in their bones and joints, whilst certain of the adults with lung disease will also acquire the infection in the spine or limbs and will then need skilled orthopædic treatment, as well as sanatorium conditions.

Between the wars the orthopædic schemes were particularly successful in preventing deformities in cases of "surgical" tuberculosis and in putting the healed individuals into industry, even in heavy jobs. Many indeed joined the army, but whether their contribution to it was worth the risk of lighting up so dangerous an infection is a subject for study by military medical officers. These successful results were attained by prolonged in-patient treatment, followed by equally prolonged supervision in out-patient clinics, with adjustment when possible of unfavourable factors in the home and school environment. Because deformity (though not a stiff joint) can be prevented in tuberculous cases, it does not mean that any method has been discovered of healing them in a short time, nor without skilled nursing and skilled surgery. Certain operative procedures, like the fixation of joints which have become stiff without final stability, do guard against relapses due to strain, but they only form one and almost the final stage of a continuous, prolonged plan of treatment. Far from shortening this, as was once hoped for the spine-graft, if they are carried out prematurely they result in most dangerous flares-up of the infection, which take even longer to subdue.

It can be roughly reckoned that two years is the minimum time in which a child's bone or joint tuberculosis can be mastered, and many take four, five or even more years. On the whole, contrary to what is sometimes supposed, adult surgical tubercle heals in a somewhat shorter period, although no two cases are alike.

Poliomyelitis (infantile paralysis) is a disease that appears to be on the increase, although some of this may be due to more accurate diagnosis and the greater alertness of the profession to recognize the disease in the acute phase and to bring it under orthopædic treatment before the paralysed muscles have been overstrained in their vulnerable stage, rendering their loss permanent. The above remarks in regard to the treatment of tuberculosis apply equally to poliomyelitis, i.e., that early diagnosis does not guarantee early recovery, although it does ensure complete recovery in a high proportion of cases, even some which looked most unfavourable for a time. Similarly, the avoidance of ultimate deformity demands the most skilled nursing and absolute persistence in supervision, for

most of the deformities, like scoliosis and claw-foot, are insidious in onset and need considerable experience for their detection in the stages when complete prevention is possible. Indeed, scoliosis is apt to follow mild degrees of weakness in a whole series of muscles, such as the glutei, parts of the erector spinæ, or one side of the abdominal wall, particularly if the limbs are strong and the patient is able to indulge in violent activity and so resents any restraint. As with tuberculosis, operative surgery should only be resorted to as a supplement to other measures and in the late stages.

When it is considered that the maximum probable recovery has taken place, the total function of the child as a whole should be assessed and thereafter a decision reached whether any form of operation will add to his efficiency. The most useful, and most widely used, of such measures is the triple arthrodesis of the foot, either the Dunn technique or its modifications, whereby the tarsal bones are induced to fuse into one mass, which moves through a moderate range at the ankle, but is prevented from lateral instability at the subastragaloid joint, or from dropping into a cavus condition in the middle, whether at the tarsal or metatarsal joints. Lambrinudi pointed out that if the bones are cut at a suitable angle, the plantar flexion of the ankle also will be limited sufficiently to compensate for paralytic foot drop. Occasionally, some supplementary device of transplanting tendons, or putting a bone block behind the ankle, is also indicated.

The transplanting of strong tendons into weak ones, which had a great vogue at one time, is now strictly limited to certain regions, chiefly non-weight-bearing ones, such as the great toe, or thumb, since the active muscle often proved to be less normal than supposed and failed to develop enough in its new function. Conditions were different with gun-shot wounds, which had destroyed one tendon or nerve in an otherwise normal limb, then the transplanted muscle could be expected to develop to much more than its original bulk when new duties were imposed on it. In poliomyelitis it is probable that a large percentage of all the muscles are affected in varying degrees, and therefore if early strain of the whole organism is not avoided and activity resumed very cautiously, late deformities will occur or even apparent relapses. Before cases reached hospital in the acute, febrile phase, it was a common history to hear "he seemed all right for a week, then suddenly one leg gave way." Often this unexpected giving way followed a walk up-hill, or a game of football, no doubt the muscle was already paralysed in part of its fibres and the strain overstretched the rest. Therefore, it is wise to admit to hospital the mildest cases and limit their activities before discharging them. If isolation rooms and barrier-nursing are available it is desirable to admit them direct to an orthopædic hospital, as fever-staff cannot be expected to be expert in detecting early muscle defects, whether atony or spasm, or in splinting them at this stage. In twenty years' experience at the Bath and Wessex Orthopædic Hospital, no case of prolonged joint stiffness has resulted from early splinting, whereas many have been seen at the clinics in cases untreated for a long period after the onset, or splinted without regard to balance of the limb as a whole. Undoubtedly many of the cases of stiffness for which non-medical therapists have blamed the medical profession, have been cases of an associated arthritis, which occurs in certain epidemics and was described many years ago and again recently.

by the late Dr F J Poynton This arthritis, whilst a cause of early stiffness, yields like other forms of acute arthritis to rest in plaster or other well-fitting splint, and after judicious physiotherapy gives full mobility As remarked already, it is found in cases which had no early treatment at all, whether lay or medical, and in such could not be attributed to splints

Congenital defects of limbs and spine might possibly have been expected to be reduced by schemes of ante-natal care, but unfortunately this has not proved to be the case, and such conditions as club foot (equino-varus), dislocation of the hip and spina bifida still put a heavy burden on orthopædic schemes, for they seem even more obstinate in their resistance to treatment than the infections referred to above What is often forgotten is that a child's bones and muscles and other growing tissues obey the same laws as do trees and other plants It is not surprising to find the young tree arching at the behest of the prevailing wind and the old gnarled trunk bent irreparably, yet many are surprised to find a knock-knee increasing, instead of "being grown out of," when the child walks daily on an unyielding pavement on the inner strap of a sandal which offers no grip to the foot muscles and allows the inner border of the foot to lie constantly on the ground If the weakness of the inner arch muscles happens to be congenital, a common condition of mild amyotonia of the whole lower limb with slack calf muscles and hamstrings also, then the child will reach adolescence with great splay-feet pointing outward from the hip, and cure by conservative measures will be almost impossible Conversely, if the mother brings the infant to the clinic, and if she carries out the exercise of arching the feet and inducing active inversion by tickling the arch muscles at their insertion, good arches will form, although when the child first walks it will still need firm boots and inside wedges to heel and sole, and such wedging may need to be continued for years In the reverse condition of equino-varus, although the new-born foot can be moulded without anæsthesia into over-correction, yet the peronei may fail ever to develop enough power to evert the foot and, although by walking-irons and the Denis-Browne splint at night the feet may be coerced into growing a good shape, yet it may ultimately be necessary to regard the foot as a condition of peroneal paralysis and fuse it by the Dunn operation Such fusion will not prevent bone yielding like the young tree, if it is done much before the growth of the foot is finished, therefore it is desirable to wait until after ten or twelve years of age.

Congenital dislocation of the hip should be suspected and excluded by X-rays in any young infant with even slight asymmetry of the lower limbs, but even the X-ray needs experience to interpret it at this age, as it was demonstrated by Putti of Bologna that many ill-formed hip-joints were not actually dislocated until weight was put on them when the infant first walked They can be reduced in infancy by persistent abduction on a simple splint, but again persistence is essential

Congenital scoliosis is another condition which cannot be treated too early or too thoroughly If the surgeon waits until the child walks, gross bone deformity will remain for life If it is recognized when only slight bulging of the ribs on one side is present, it can be cured by keeping the child day and night on a padded wooden bed with one crutch against the convexity and two to counter-press the opposite side

From the remarks on page 245 it will be evident that most of the treatment of congenital defects can be carried out in orthopædic clinics, provided there is a keen, skilled staff and also control of a workshop where splints are made to the surgeon's specifications. Keeness in the staff is essential in order to induce patience and persistence in the parent.

In passing, it may be mentioned that defects due to trauma at birth can also be handled in such a clinic, provided they attend soon after birth. Such are wry-neck, which yields to a simple cap and elastic band, Erb's birth palsy, which only requires a strip of vulcanite to keep the arm vertical in an infant too young to sit up or wriggle much, transitory foot-drop, which can be splinted with cardboard and strapping.

OTHER CAUSES OF CRIPPLING

Other bone and joint conditions which add to the work of an orthopædic scheme include various obscure types of *arthritis* of the joints, the milder ones of which can be splinted at clinics. Unfortunately, these include many "sprains" and epiphyseal injuries, and also adhesions following injury, which were overlooked or dismissed as trivial when some fracture had united in good alignment. It is no more true of children than adults that good X-ray union of a fracture is identical with normal function of a limb. Few need definite occupational therapy, most need a carefully calculated manipulation, mostly without anæsthesia, a few need further splinting. The frequency of this group proves that either a fracture service should be run in close association with an orthopædic scheme, or as part of it. Yet this aim does not seem fashionable at present.

Rheumatoid arthritis, if treated with as long and judicious splinting as tuberculosis, gives surprisingly good functional results, but in a late, half-treated stage with contractures it is depressing to handle.

Various causes of *bone-softening* exist besides rickets, such is cretinism, which soon yields to thyroid medication, but may need leg splinting to prevent deformity while the bones are hardening. This applies also to the fairly common condition of pituitary dystrophy, which is a great source of severe knock-knee, and later predisposes to slipping of the upper femoral epiphysis and severe kyphosis in adolescents. In young children thyroid in large doses seems to whip up the pituitary and is a cheap form of treatment, injection of whole pituitary gland is also effective, but expensive and tedious.

Congenital syphilis with softening of the metaphyses is another source of deformity of rickety type, the bones soon harden with grey powder and other anti-syphilitic drugs, but often the severe bow at the end of a long bone will not respond to splinting and it is necessary to re-soften the affected region by boring a series of holes with a sharp awl through a skin puncture, and then the bone can be reshaped as easily as a melted candle.

Spastic conditions of the limbs and other cerebral palsies, such as athetosis, can also be treated almost entirely in the clinics, provided the patients are taken on in infancy before they have formed wrong habits of walking. The children with spastic hemiplegia can be made to walk normally and use the affected hand almost

normally by a series of rhythmic exercises in hot water, provided the mother carries these out. If she is unable to do so, they should be treated in a warm pool in hospital and by hand-work under an occupational therapist. The ordinary school teacher, even in a school for cripples, seldom has time or sufficient knowledge of anatomy to handle them.

ORGANIZATION OF AN ORTHOPÆDIC SCHEME

After this bird's-eye view of the conditions which cause crippling in children and of the therapeutic measures required to deal with them at the earliest possible moment, it is possible to review briefly the essential features of an orthopædic scheme. It is to be hoped that in the coming reorganization of medical services, the schemes which had these features will be able to maintain them and those which were incomplete to fill their gaps. In all branches of human activity it has often been shown that rapid reforms carried away in their flood-tide a number of benefits, which had been the acceptable products of slow evolution.

The two essential parts of an orthopædic scheme are —

(1) A central hospital, with a specially trained medical staff and specially trained nursing staff, there should be a proportion of about one nurse to three patients, as the care of splints, the washing and feeding of helpless cases and the production and repair of plaster-of-Paris splints are all time-taking processes.

(2) A circle of orthopædic out-patient departments, which in a rural area should be situated in all or nearly all the market towns, as these are well served by local buses and trains. No patient ought to have to travel more than about ten miles to a clinic. The clinics should not be so remote from the hospital that they cannot be reached by the surgeon easily in a car without excessive loss of time on the road. The actual radius varies with the type of road and car. In the United States, seventy miles is considered quite near for a surgeon to visit a hospital to operate, as he does the distance in, or nearly in, an hour on the straight, wide road. Few British roads lend themselves to this time-table.

CENTRAL HOSPITAL — This must provide for *open-air* treatment, which is essential for the tuberculous cases and beneficial for all others. Rickety infants, subject to bronchitis, ought to be able to sleep in some warmth, so their ward should have a closed part; acute poliomyelitis cases have very cold extremities and also need some protection from wind, so that a verandah ward is improved by some form of sliding door, which leaves room for ventilation at the top, but can be partly or wholly closed along the ground, it should have glass, so that winter sun in windy weather, or after a snowfall, can penetrate and its warmth be trapped.

The hospital must have a first-class *operating theatre* unit and large plaster-room with first-class staff, for the more complicated orthopædic operations are some of the most exacting in surgery. There must be ample room for cases with their limbs widely abducted to pass through the doors without tilting the patients heaving them about increases shock.

A *splint-workshop*, where apparatus can be made to the surgeons' own designs, is also essential and adds to economy of running cost. It should make all the apparatus prescribed in the clinics.

NOTES AND QUERIES

CLIMATE AND CHRONIC RHEUMATISM

QUESTION—A general practitioner who has been in a colliery practice in South Wales for the last thirty-five years is about to retire. He is subject to rheumatism. What part of the British Isles could you recommend him to retire to?

REPLY—Sufferers from chronic rheumatism, whether articular or non-articular, are profoundly influenced as regards their symptoms by weather changes. They are apt to experience most discomfort at the time of the actual change, or, as it is often called, "the weather front," so much so that the French apply the term "barometrique" to this susceptibility. A dry, equable climate is therefore ideal for such conditions but this is unfortunately never attained in the British Isles. If a pointer be laid diagonally across a map of Great Britain it will be found that the western half has a relatively greater rainfall than the eastern, and for that reason the drier counties of Kent, Essex, Norfolk and Suffolk are preferable as places of residence for rheumatic subjects. Speaking generally, the sea-coast does not suit such individuals so well as places farther inland at a somewhat higher altitude. The question of the mean average temperature is not of so much importance as the average rainfall, which may vary from 20 inches in the drier parts of the country to 120 inches in the Lake district and Western Highlands of Scotland.

MATTHEW B. RAY, D.S.O., M.D.

ALLERGY AND RHEUMATOID ARTHRITIS

QUESTION (from a reader in Manchester)—Professor L. S. P. Davidson, of Edinburgh, in an article in the *Glasgow Medical Journal* of December 1943, has stated that an allergic reaction may be regarded as a possible cause of rheumatoid arthritis, and used as a working basis for prophylaxis and treatment. Should adrenaline and/or pituitrin be used therefore in the treatment of the acute stage of the disease? and should gold be used in the acute stage if the patient is running a temperature for several days or weeks?

REPLY—As the cause of rheumatoid arthritis is unknown, my suggestion that the clinical features could be explained on an allergic basis must be regarded merely as a hypothesis, for the supply of both clinical and experimental evidence that any value in the use of these drugs. With regard to the use of gold, it should be used if the patient has rheumatoid arthritis.

theoretical grounds it might be wiser to delay treatment with gold for a few weeks if the patient had much fever. Should the pyrexia, however, not abate on the systematic treatment, including rest, I would be prepared to advise gold therapy when the other indications were in its favour.

L. S. P. DAVIDSON, M.D., F.R.C.P.

NUTRITIONAL ŒDEMA IN INFANTS

QUESTION (from a subscriber in S. Africa)—I am rather worried about the treatment of nutritional œdema in infants which is frequently seen in these parts. A fair percentage respond to treatment with vitamin extracts but others make no response at all. In the latter case I have tried nicotinic acid by injection, vitamin B complex, liver extract, high protein diet, and so on, all together or at different times but with no response whatsoever. I have used particularly large doses of nicotinic acid because of the pellagra-like dermatitis so often seen in these cases. Is there anything else you could suggest for the treatment of this condition in children, especially under the age of two?

REPLY—Admittedly the treatment of œdema in infants under the age of two is unsatisfactory because of the difficulty in finding out the true cause, and this experience is general. The serum proteins will probably be reduced, whatever the etiology, and it is suggested that the mechanism responsible for their manufacture may be temporarily out of order. A complete history and physical examination, with special attention to the urine (albumin and chlorides), is helpful in the differentiation of those who respond to vitamin extracts and those who do not. It is presumed that in the majority of instances the infants are marasmic and perhaps suffering from a variety of diseases associated with infantile diarrhoea. Often the œdema appears after the diarrhoea has cleared up, in which case treatment should be directed to making the infant thrive by increasing the diet gradually to the full caloric requirements. High protein diets of good quality are recommended. The addition of casein to the feed is the simplest, or Finkelstein's protein milk may be used. Saline, of course, should not be given. If pellagra is suspected—and it seems a possibility if there is a dermatitis of pellagra-like distribution—the B complex rather than nicotinic acid is indicated. Massive albuminuria, of course, is a possibility of nephrosis, a condition which occurs in the second year of life and in the first twelve months. The prognosis will be the same as in older children.

M.R.C.P., F.R.F.P.S.

PRACTICAL NOTES

THE DIET IN PREGNANCY

UTRITION in pregnancy is no more exempt from the attention of the faddist than any other part of this fashionable branch of medicine, and a review by C. J. Lund (*Journal of the American Medical Association*, June 2, 1945, 18, 344) focuses attention upon how much of present information is based upon experimental evidence (either human or animal) and how much upon empirical teaching. The optimum daily diet in pregnancy should consist of one generous helping of meat (liver should be taken at least once weekly), one quart of milk, one egg, one ounce of butter, one fresh vegetable, one green leafy vegetable and one other cooked vegetable, citrus fruits and wholemeal bread. With such a diet the only supplements required are vitamin A, 5,000 IU during the first trimester and 10,000 IU during the third trimester, and possibly vitamin K during labour up to the new-born infant. This diet provides 3,000 calories daily, which is sufficient unless the woman is doing heavy work, when the total caloric content should be raised to 2,500 calories by means of extra carbohydrate and fats. Care must be taken to ensure a sufficient intake of first-class protein, as the old superstition dies and that "protein is bad for the pregnant mother." One quart of milk supplies 12 gm of calcium, and, as the optimum intake during pregnancy is probably 15 gm. daily, there is obviously no need for the administration of extra calcium salts. Unless there is any evidence of anaemia in the early stages of pregnancy there is no need to give iron in addition to that contained in the diet. Whilst there is no necessity to give supplements of the water-soluble vitamins (B and C) in an uncomplicated pregnancy, it is often forgotten that any infection may deplete these vitamins, it is therefore essential to give additional amounts in the presence of infection. Serious and prolonged vomiting, as in hyperemesis gravidarum, also results in a deficiency of vitamins B and C.

INTRAVENOUS NICOTINIC ACID IN PERNICIOUS MALARIA

ON the basis of the successful results reported on the vasodilator action of intravenous injections of nicotinic acid in cerebral thrombosis, angina pectoris and Ménière's disease, Capt. B. S. Dhillon, Capt. J. H. Joshi and Capt. S. K. Roy (*Journal of the Royal Army Medical Corps*, June 1945, 84, 268) have treated two cases of pernicious malaria (coma), one with a massive dose of nikethamide in conjunction with quinine

bihydrochloride, and the other with 200 mgm. nicotinic acid in one pint of sterile physiological saline, given at a rapid rate. In this second case there was a dramatic response, the patient regained consciousness within thirty-five minutes of the start of the nicotinic acid drip, subsequently, he was given one intramuscular injection of atebirin musonate (4½ grains) and routine treatment for malaria. In the first case the patient on admission was unconscious and did not respond to painful stimuli, he was given intravenous quinine bihydrochloride, 4 grains, four-hourly, up to 12 grains total dose, and intravenous nikethamide 3 c.c.m., repeated every thirty minutes up to 45 c.c.m. total dose. A tracheal tube was passed and plugs of mucus sucked out by catheter. The patient recovered consciousness twelve hours after the institution of treatment, and no untoward after-effects were noted.

THE SIGNIFICANCE OF POLYMORPHS IN THE GALL-BLADDER

As the result of a careful investigation of a controlled series of over 100 gall-bladders, J. P. McKibbin and J. R. McDonald (*Proceedings of the Staff Meetings of the Mayo Clinic*, May 30, 1945, 20, 167) conclude that the presence of polymorphonuclear leucocytes in the wall of the gall-bladder is not by itself a sign of inflammation. Their series included thin-walled, non-calcareous gall-bladders, "strawberry" gall-bladders and calcareous gall-bladders, and in every instance polymorphs were found in the wall of the gall-bladder, although they were more abundant in the "strawberry" gall-bladders than in the others. They were also found in the walls of the ten gall-bladders removed from dogs at the time a heart-lung preparation was being made. They were not found in ten gall-bladders removed from fetuses. The suggestion is made that possibly these polymorphs subserve a metabolic rather than an inflammatory function.

FOLIANDRIN IN THE TREATMENT OF HEART FAILURE

A REPORT of the results obtained by the use of a cardiac glycoside extracted from the leaves of *Nerium oleander* (foliandrin) is given by S. Btsh (*Acta Medica Orientalia*, June 1945, 4, 192). Particulars of six cases are given, in which special attention was paid to the action of the glycoside on auricular fibrillation. In one case, a girl of sixteen with congestive heart failure, mitral stenosis and auricular fibrillation, foliandrin was

given in dosage of 50 drops in the morning and 30 drops in the evening. Six hours after the first dose the apical rate dropped from 130 to 95 beats per minute, and there was an increase in the urinary output. The drug was then administered twice daily, the dose being regulated in accordance with the pulse rate. There was rapid recovery, and the patient was completely compensated in one week. Equally good results were obtained in the case of a seventy-year old woman with auricular fibrillation, congestive heart failure and cirrhosis of the liver. Folandrin was given in initial dosage of 50 drops daily and increased up to 150 drops daily. There was rapid diuresis and slowing of the ventricular heart rate, and on the ninth day after admission the patient was completely compensated. From the observation of these and other cases the author notes two striking facts—(1) the effect of the oleander glycoside on the pulse rate in auricular fibrillation can be registered within a few hours of its administration, the action resembling that of strophanthin rather than digitalis, which requires

certain period of accumulation before the action becomes apparent, (2) the strophanthin effect is obtained by the oral administration of the oleander glycoside, which presents the advantage that the drug is quickly absorbed and eliminated from the organism. After considerable trial it was found that the optimum mode of administration was to divide the daily dose into three parts, given at six- to eight-hourly intervals, but the exact dosage was based on the individual case. It was found that the optimum response was obtained by the administration of 150 drops in twenty-four hours (approx. $3\frac{1}{2}$ to 4 cat units), but this amount could not be continued for more than two or three days or toxic signs appeared. The dosage was lowered as soon as a satisfactory response was obtained, i.e., diuresis and slowing of the heart, and once compensation was established maintenance was obtained by giving 15–20 drops, twice or thrice daily. Mild cases could be kept compensated with a single daily dose. The most common sign of intolerance or overdosage was diarrhoea, which improved immediately on stoppage of the drug. Another important sign of overdosage was the appearance of extrasystoles, but no case of actual bigeminal pulse was noted.

REQUIREMENTS OF VITAMIN A

THE Vitamin A Sub-Committee of the Accessory Food Factors Committee has just completed a two-years' investigation of the requirements of vitamin A in man. These experiments were carried out on twenty-three conscientious objectors who volunteered for the purpose. A full report is to be published in due course, but in order that the practical results may be known as soon as possible, a preliminary report

has been issued (*Nature*, July 7, 1945, 156, 11). The Committee considers that inclusion in the daily diet of 2,500 I U vitamin A or of 5,000 I U carotene can be regarded as adequate for the maintenance of normal adults and also leaves a fair margin for safety. It was found that it was only after twelve to twenty months' deprivation that definite signs of vitamin A deficiency appeared in the subjects of the experiment. As the body reserves of vitamin A have a mean value of 600,000 I U, this would correspond to an average rate of consumption of 1,300 I U daily for fifteen months.

THE SMOOTH TONGUE

THE old theory of the diagnostic value of the coated tongue has lost much of its significance since Fuchs, in 1898, showed that this was purely a local phenomenon due chiefly to reduced mechanical cleaning of the tongue, and that the coating increases during anorexia, such as is associated with acute gastritis. That a tongue with a smooth, atrophic mucous membrane may have some diagnostic significance, however, is shown by M. Faber (*Acta Medica Scandinavica*, 1945, 121, 179), who has observed fifty-one patients, all with complete or partial atrophy of the mucous membrane. This atrophy is characteristic in appearance, in the milder cases, symmetrical 1 cm patches, with no papillae, are present on the dorsum linguae; on the remainder of the tongue the papillae are usually small, and there is scarcely any coating. In the more severe cases the lack of papillae is observed over larger areas, and in the most severe cases there is a complete lack of filiform papillae, the mucous membrane being absolutely smooth, giving the tongue the appearance of a glazed surface. In severe cases, especially those of long duration, the surface is less smooth and has a "nubbled" appearance, and the epithelium is so dry that wrinkles appear when the tongue is pressed with a spatula. In these severe cases the tongue is bright red, even if the patient has a pronounced anaemia, and the bright red colouring and glazed appearance are also present on the internal mucous membrane of the cheeks. Of the fifty-one patients examined, nine had pernicious anaemia, seven iron deficiency anaemia, four the Plummer-Vinson syndrome, ten gastric achylia without anaemia, three arboflavinosis, two diabetes mellitus, four sialoadenitis chronica, seven xerostomia cryptogenica without gastric achylia, and the remaining three cancer ventriculi, non-tropical sprue and aphthous stomatitis, respectively. Except in the case of aphthous stomatitis, in which the cause was local, the salivary secretion was reduced in all cases, in contrast with what is found in other types of glossitis in which salivary secretion is normal or increased. It was found that when

rose to normal values the mucous of the tongue resumed its normal and on the basis of this and other the author concludes that the atrophy of the mucous membrane of the tongue be due to xerostomia

1. LATENT PHLEBITIS AS A CAUSE OF ARTHRITIS

In an article dealing with latent phlebitis and arthritis, O Meyer (*Schweizerische Medizinische Wochenschrift*, July 21, 1945, 75, 639) states that infection from endophlebitic disturbance in the circulation plays an important rôle in the genesis of inflammation of the joints. A joint that becomes defectively drained as the result of inflammatory phlebo-stenosis in the efferent veins, falls victim to venous congestion, the destructive results of which are accumulation of effete matter, increased transudation due to venous pressure, increased permeability of the smaller veins and capillaries and, finally, stagnation anoxia. Local lack of oxygen in the obstructed area seems to be the most important factor in the reduced local resistance. The diagnosis of latent deep phlebitis can only be made by palpation of the veins in relaxed muscles; in many cases definite induration of the wall of a vein can be felt. Treatment consists first in eliminating the focal infection, and, since peripheral phlebitis frequently has its origin in the jugular veins, it is most important that foci of primary infection in the teeth and tonsils should be completely removed. The author places emphasis on the word "completely". Frequently patients who have had their tonsils removed, retain a residual lower pole, and it must be borne in mind that the smallest residual portion of an infected tonsil is a classical example of a focal infection. Because no local symptoms are present such a residual focus can easily be overlooked. After removal of the primary focus, in many cases sensitiveness of the jugular veins disappears, but if jugular phlebitis persists, leeches should be applied over the course of the jugular and subclavian veins. Inflamed hamorrhoids may also act as foci of infection. In the treatment of deep phlebitis of the leg the best results can be obtained by the use of compression bandages. When the joints of the foot are inflamed the bandage should be applied below the knee, when the knee joint is involved, above and below the knee. The best bandage is a combination consisting of a strip of Uma's paste bandage applied with slight pressure, and over this an 8 cm. wide elastic adhesive strapping. As the inflammation and swelling quickly subside, the bandage becomes loose, and must be frequently renewed until the

sensitiveness to pressure of the deep veins has quite disappeared. This method of treatment not only removes the congestion and stagnation anoxia of the tissues, but facilitates a flow of fresh arterial blood, which is the best measure for the removal of infection. Application of the pressure bandage to the inflamed proximal veins, immediately lessens the pain in the distal joint, and dispersal of the proliferative endophlebitis leads to recalibration of the excretory veins and thereby to decongestion of the inflamed joint.

THE MODIFIED METHYLENE BLUE TEST IN INFECTIVE HEPATITIS

CAPT S S GELLIS and J Stokes, Jun (*Journal of the American Medical Association*, July 14, 1945, 128, 782) report on the use of a modified form of Franke's methylene blue test, in a series of seventy-seven patients with hepatitis, thirty-three of whom were in the pre-icteric stage. The test was as follows—2 drops of an 0.2 per cent aqueous solution of methylene blue chloride were added to 5 c.cm. of pre-breakfast urine. If the resultant colour was green, more drops of methylene blue were added and the last drop required to convert the green colour to blue recorded. A test of 5 drops or more was considered positive. Pipettes which delivered 20 drops of solution per c.cm. were used. If more than 5 drops were required to produce the colour change the urine was diluted with distilled water, and methylene blue again added drop by drop until the end-result was obtained, correction was then made for the dilution factor, which was rendered necessary, as after more than 5 drops of methylene blue had been added the resultant colour was of such intensity that the end-point was difficult to determine. The tests were carried out daily. In the thirty-three pre-icteric patients the test became positive one to six days before scleral icterus appeared. At the time when the test first became positive, twelve of the thirty-three patients had normal icterus indices, the remaining twenty-one showing either indices at the upper limits of normal or slightly elevated. The test was also found of value in following the course of the disease. In the seventy-seven patients studied the range of icterus index in which the test became negative was between 35 and 20. Five patients in the series of seventy-seven developed relapses, in all five the methylene blue tests again became positive. In conclusion, it is stated that the test proved of value in the early diagnosis of pre-icteric hepatitis, in evaluating the course of the disease and in predicting impending relapse. The simplicity of the test commends its use in large-scale testing during epidemics of infective hepatitis.

REVIEWS OF BOOKS

Leukopenia and Agranulocytosis By WILLIAM DAMESHEK, M.D. Oxford University Press, London Humphrey Milford, 1944. Pp vi and 70 Price 10s 6d

THIS monograph is a reprint of two chapters from the latest edition of the "Oxford Loose-Leaf Medicine." The literature is critically reviewed up to the end of 1943. All aspects of the subject are adequately covered, but the section on the treatment of agranulocytosis is particularly well balanced. The author believes that pentnucleotide and other allied treatments have not given the results originally claimed for them. The ideal treatment, he considers, consists in, first, discontinuation of the causative drug; secondly, symptomatic care, thirdly, control of the sepsis by sulphathiazole or penicillin, and further, on theoretical grounds, the administration of viable leucocytes by transfusion from a case of chronic myeloid leukaemia. It may be mentioned that those who have tried this latter treatment have not had much success. The author also believes with Plum that the bone marrow picture of "maturation arrest," found in many cases of agranulocytosis, is rather a sign of beginning recovery than a cause of the disease. It is somewhat surprising in the chapter on leucopenia to find a leucocyte count of 5000 to 6000 per c mm designated as "border-line leucopenia" and from 4000 to 5000 as "fairly definite leucopenia." The format of the book is excellent and the text free from errors, the only one found being "kala-agar" in the index. This book may be recommended to all as a stimulating review of the subject.

Cleft Palate and Speech By MURIEL E. MORLEY, B.Sc., F.C.S.T. Edinburgh E. & S. Livingstone Ltd, 1945. Pp. xii and 160. Figures 52. Price 7s 6d.

THERE are so many aspects of the difficult problem of obtaining a first-class functional result in the repair of the cleft palate that it is only natural that many people with diverse interests should be concerned in it. There is something in this book for everyone who has any contact with such a patient. The excellent chapters on the anatomy and function of the palate are of equal value to the speech therapist and to the surgeon. The resumé of the operative procedures which have been used in the past in an attempt to cure the deformity, leads naturally to a description of the present-day procedures. Whilst it is true that this aspect is primarily of

surgical interest, there is much to be said for its inclusion in a book which is designed to appeal to the speech therapist. It at least gives a clear understanding of the technical difficulties with which surgery is fraught. The procedure as described by Wardill receives pride of place. This is only natural, as the author has had the very great advantage of working with him and of reviewing his cases over a period of years. If there must be criticism, it might be suggested, that more credit should go to the anaesthetist, upon whose skill the surgeon is so largely dependent. It is probable that it is almost entirely due to his increased efficiency that the mortality rates, particularly in young children, are showing a steady fall. Indeed, it may well be that the figures quoted, which are now twelve years old, by no means give a true picture of the present state of affairs. Thus, however, is a minor criticism of a book which for the first time, it is believed, presents the salient points of the many aspects of the problems which confront the surgeon in his endeavours to produce a functional oro-nasal sphincter, and the speech therapist in her efforts so to supplement these results that speech defects are eliminated.

Proctology By SYLVAN D. MANHEIM, M.D. Oxford University Press, London Humphrey Milford, 1945. Pp vii and 137. Price 12s 6d.

THIS small book, one of the "Oxford Medical Outline Series," is written in precis form, comparable to the notes students make for themselves in recording their knowledge. It contains no diagrams or illustrations, and no discussions on controversial points, but is conveniently interleaved with blank pages intended to be used for supplementary notes. The information given on the diseases commonly met with in a rectal out-patient clinic and the treatment given in this department is easy to read, concisely expressed and quite adequate. Thus both the out-patient dresser and the general practitioner will receive help in good measure. The student concerned with in-patient treatment will also find much to appreciate, but he is left ill-informed on some subjects to which as a rule he devotes considerable thought. The treatment of the high-level fistula is not considered. Few will be satisfied with the chapter on anaesthetics, and that on colostomy leaves many gaps. In this country, at any rate, most surgeons prefer the *Silac* colostomy to the one through the rectus, recommended by the author—but this difference in

procedure is perhaps not important. On the other hand, the practice of opening the routine colostomy immediately saves the patient many days of distress, and is steadily replacing that of leaving the colostomy unopened for four to six days, which the author advocates. In the treatment of cancer, the case for the perineal excision for anal and low-rectal growths is poorly presented, and the advantages afforded by the lithotomy-Trendelenberg position for the more formidable combined (abdominal and perineal) procedure necessitated by pelvi-rectal growths should entitle this technique to a brief note.

Getting to Know your Baby By D W WINNICOTT, F.R.C.P. London William Heinemann (Medical Books) Ltd, 1945
Pp 27 Price 1s

This is a delightful little monograph written in the vein of a friendly homily to prospective and young mothers: father is included too. The author tackles many important problems in a most helpful manner. In a postscript at the end the subject of education of parents by the State is discussed, and the importance of those in the public services recognizing the mother's knowledge of her child. In Dr Winnicott's words "the State is indeed wise in its policy of education of parents with non-compulsion, and the next step is education of those who administer public services, and the deepening of their respect for the ordinary mother's feelings and instinctual knowledge in regard to her own children."

NEW EDITIONS

Recent Advances in Neurology and Neuropsychiatry, by W RUSSELL BRAIN, D.M., F.R.C.P., and E. B. STRAUSS, D.M., F.R.C.P., in its fifth edition (J. & A. Churchill Ltd., 1945) appears for the first time under its new title, and with the incorporation of the subject of neuropsychiatry the combined authorship, which was suspended for the fourth edition, is resumed. In the preface to the new edition a description of the meaning of the term "neuropsychiatry" is given, and an explanation of its adoption on the basis of the interrelationship of many mental and neurological disorders. The book has been almost entirely rewritten, and much new material has been added, including electrical convulsant therapy in mental disorders, prefrontal leucotomy, thymectomy in myasthenia gravis, the use of penicillin and the sulphonamides in meningitis, and a number of other advances. The chapter on electro-encephalography has been considerably extended, and the chapter on injuries of the brain rewritten in the light of war experience.

The second edition of *Introduction to Diseases of the Chest*, by JAMES MAXWELL, M.D., F.R.C.P. (Hodder and Stoughton, 12s 6d) concludes with a useful selection of X-ray illustrations printed as negatives, so that they may be more readily comparable with films seen in actual practice. Although the grouping together of illustrations in this manner is a war-time expedient due to paper difficulties, the result in this instance is most happy, as it gives the student the opportunity of comparing the films and noting the differences to be observed in the X-ray appearances in various diseases of the chest. These are discussed in detail in the chapter on radiology, which also contains sections on diagnostic pneumothorax, tomography and kymography. The technique of artificial pneumothorax is given in the chapter on the treatment of pulmonary tuberculosis, and other sections of interest are those on pneumoconiosis, silicosis, asbestosis, siderosis and anthracosis. The clear exposition of diagnostic signs, as well as measures for treatment, including some useful formulæ, commend this new edition to the notice of the practitioner.

New chapters on erythroblastosis, vitamin K, still-birth and neo-natal death, and nutrition in pregnancy are included in the sixth edition of *Recent Advances in Obstetrics and Gynaecology*, by ALECK W. BOURNE, M.B., Ch.B., F.R.C.S., F.R.C.O.G., and LESLIE H. WILLIAMS, M.D., M.S., F.R.C.S., F.R.C.O.G. (J. & A. Churchill Ltd., 1945). A separate chapter has also been devoted to the subject of X-ray therapy, which was formerly included in the chapter on radiology. Other features of interest are a section on artificial insemination, and another on the use of dicoumarin for the prevention of venous thrombosis. The illustrations in this new edition are delightfully clear, particularly those of X-ray films.

Intravenous Therapy, by K. V. THAKKAR, L.V. & S., in its second edition (K. V. Thakkar, Bhavnagar, Bombay Presidency, Rs 8/8) presents this somewhat complicated subject in a most comprehensive manner. After a general consideration of intravenous therapy, the author proceeds to the discussion of apparatus, sterilization, the technique of injection, the choice of vein, dangers and their avoidance, different solutions used, and indications and contraindications. There is a useful chapter on intravenous anaesthesia and another on blood transfusion. The inclusion of a number of new drugs, with their dosage and mode of administration, is a feature of the new edition, which appears only eighteen months after the first publication of the work.

NOTES AND PREPARATIONS

NEW PREPARATION

FLAVAZOLE is a chemical compound containing equimolecular proportions of 2,8-diamino-acridine (proflavine base) and sulphathiazole, which experimentally has been shown to be active against *Proteus*, *Cl. welchii* and *Ps. pyocyaneus*. Clinical trials, in which the new antiseptic was used as a compound powder (2 per cent flavazole and 98 per cent sulphathiazole) and also as a saturated aqueous solution (1:2500) in the treatment of heavily infected open wounds are stated to have shown a 50 per cent. success rate, and healing by first intention was obtained in 100 per cent. of cases of cartilage grafts and rotation flaps when no infection was present. Flavazole, in the form of a sterilized compound powder (2 per cent. flavazole, 98 per cent. sulphathiazole), is supplied in cartons of 12 sifter packets of 5 gm., price 13s 5½d, and in bottles of 15 gm., price 3s 6d, and Flavazole in bottles of 25 gm., price 14s 11½d, by Boots Pure Drug Co., Nottingham, from whom descriptive literature can be obtained.

NEW APPARATUS

PRECISION MICROTOMES of types hitherto not manufactured in this country are being placed on the market by the Machine Shop Equipment Ltd., Allington House, 136-142 Victoria Street, London, S.W.1. The first two models available will be the Base Sledge Microtome and a small Freezing Microtome with automatic feed, the knife being held between vertical centres. Further particulars can be obtained from the manufacturers.

LANTERN LECTURE ON OXYGEN THERAPY

AN educational lecture on "Oxygen Therapy," accompanied by a series of lantern slides, which takes approximately forty to forty-five minutes to show and which deals with the history of oxygen therapy, the principles and application, and the different types of apparatus in use, can be loaned without charge on application to Oxygenaire Ltd., 8 Duke Street, Wigmore Street, London, W.1.

THE FACULTY OF HOMŒOPATHY

IN view of possible renewed negotiations with the Minister of Health, practitioners interested in, or practising, homœopathy, may wish to get in contact with the Hon. Secretary of the Faculty of Homœopathy, Dr. Agnes Moncrieff, the London Homœopathic Hospital, Queen Square, W.C.1.

NATIONAL REGISTER OF MEDICAL AUXILIARY SERVICES ORTHOPTISTS
The sixth edition of the National Register of Orthoptists has just been issued, and practitioners can obtain a copy on application to the Acting Secretary, Board of Registration of Medical Auxiliaries, B.M.A. House, Tavistock Square, London, W.C.1.

CATALOGUE OF MEDICAL FILMS

IN connexion with the above subject, Surgeon Rear-Admiral Gordon Gordon-Taylor, C.B., O.B.E., M.S., F.R.C.S., President of the Royal Society of Medicine, writes—

"A catalogue of all the medical films in Great Britain is now being prepared by the Royal Society of Medicine in cooperation with the Scientific Film Association. It would be appreciated if any persons holding films of medical or para-medical interest, who have not already been asked for details, would communicate with the Film Catalogue Royal Society of Medicine, 1 Wimpole Street, London, W.1. By so doing they would not commit themselves or their films, but would enable the catalogue to be complete."

OFFICIAL NOTICE

Liquid Paraffin Emulsion Orders—In view of increased supplies now available, the Minister of Health issued an Order on July 26, 1945, revoking the Paraffin Emulsion (Reduction of Liquid Paraffin) Order, 1941, the issued Order being cited as the Paraffin Emulsion (Reduction of Liquid Paraffin) Revocation Order, 1945.

CONTENTS FOR NOVEMBER, 1945

RECENT ADVANCES. PART II

- Surgery* By W. H. Ogilvie, F.R.C.S.
Chemotherapy By Sir Lionel Whitby, C.V.O., M.C., M.D., F.R.C.P.
Intestinal Infestations By E. H. Vere Hodge, C.I.E., M.D., F.R.C.P.
Allergy By David Harley, M.D., F.I.C.
Arthritis and Chronic Rheumatism By Douglas H. Collins, M.D.
Physical Medicine By F. S. Cooksey, M.D.
Industrial Medicine By Donald Hunter, M.D., F.R.C.P.
Rehabilitation By Harold Balme, O.B.E., M.D., F.R.C.S., D.P.H.

Child Health XVII—Physical Education and Health of the Child By Doris M. Baker, M.D., M.R.C.P.

Owing to limitation of space the article on "Arthritis and Chronic Rheumatism," by Dr. Douglas H. Collins, advertised to appear in the October issue of *The Practitioner*, had to be held over.

RECENT ADVANCES IN TREATMENT:
SURGERY

By W. H. OGILVIE, M.D., M.Ch., F.R.C.S.

Surgeon, Guy's Hospital

N account of recent advances in surgery can be no more than a summary of the writer's views. Recency and advance are mutually contradictory terms, and surgery is no longer a clearly fenced-off domain. The hollow needle and the electric scope have encouraged physician and surgeon to raid each other's territory, and the growth of specialism has brought forth a new race of regional practitioners who are neither the one nor the other. These men, like those older stylites the ophthalmologists and the otorhinolaryngologists, study the anatomy and the function and combine the medical and surgical treatment of some tissue, tract, system, or group of organs. The interest of surgical advance in recent years lies not in technical operative methods than in accessories that have helped to make surgery safer and its results better.

Shock and infection have been the chief factors limiting surgical enterprise in Lister's day. In modern war they present problems of the first importance, the solution of which must be sought, not only on scientific and humanitarian grounds, but on those of military efficiency and national survival. The grouping of scientists in schemes of coordinated research, the constant observation of mass human experiments on the questions under investigation, the readiness of business interests in many countries to share their secrets and pool their resources for the common good, all these have helped to cram twenty-five years of work and discovery into the last five years.

SHOCK

The problem of shock has not been solved, but it has been greatly simplified. Many factors associated with battle injury—fat embolism, blast damage to the lungs, acute anaerobic infection, absorption of toxins from damaged muscle—may complicate, and be in part responsible for, the clinical state of collapse following injury known as wound shock, and these factors must be considered in any leisurely survey. But for practical purposes, traumatic shock is in most cases the result of a diminution in the effective circulating volume of the blood. The diminution may be due to actual loss, or to a sudden increase in the capacity of the vascular system, the volume being unchanged or diminished to an extent that would not in itself lead to shock. In wound shock the loss is one of blood, either to the surface or into damaged tissues. In burn shock the loss is one of plasma, both from the burned surface and into the tissues underlying it. In the vasovagal syndrome, known also as primary or nervous shock, a state which may be found alone or preceding or accompanying true shock, the vascular bed is increased by widespread dilatation. The degree of shock is roughly proportional to the loss of circulating

fluid a loss of two pints leads to moderate shock, one of three pints to severe shock, and of four pints (roughly 40 per cent of the blood volume) to profound shock. Experimental work has emphasized the importance of fluid loss into damaged tissues without external loss, a mechanism repeatedly stressed by Blalock. A man can bleed to death into the thigh muscles around a fractured femur without any free hæmorrhage occurring. On the other hand, the view that shock leads to endothelial damage, with loss of fluid into the tissue spaces throughout the body in the later phases, is no longer held, and toxic factors are usually terminal.

Treatment—Shock is treated by restoring the circulating volume, and, so far as possible, qualitatively, that is, blood loss is made good by blood plasma loss by plasma. It is in the discovery of means to preserve, transport, distribute and administer these body fluids that the greatest advances have been made. Technical details would be out of place. Suffice it to say that during the advance of the Eighth Army across North Africa from Alamein to Tunis some 100,000 bottles of blood were collected in base areas, driven, flown or ferried across desert and sea, and administered in forward units with no serious reactions; that during the invasion of Normandy the American Army was supplied with blood collected in America and flown across the Atlantic, and that men in Burma received plasma prepared in three continents. The constituents of transfusion fluids can be varied for special needs, thus washed and packed red cells can be given to a man needing hæmoglobin but not fluid, and double strength plasma to another deficient in circulating proteins. Fractional separation of the blood proteins has been studied, and dried serum albumin is available in pure form. The globulin portion is used for immune sera, and the fibrinogen for hæmostatic and adhesive preparations. It is possible to foresee a time when further purification of protein fractions and the preservation of red cells may enable the surgeon to dispense from stored materials a transfusion fluid made up for particular needs, and free from the danger of transmitting the virus of serum jaundice, the one hazard that the wide use of pooled plasma has brought to light.

INFECTION

A new era in the treatment of infection opened with the discovery of sulphanilamide by Domagk, in 1935. The sulphonamide group, of which it was the forerunner, offered for the first time substances which, whether applied locally or coming by the blood stream, could damage bacteria yet leave the tissues unharmed. They established the principle of chemotherapy, foreshadowed in Ehrlich's salvarsan. Under the stimulus of war, research in chemotherapeutic substances has proceeded apace. Whereas in 1939 only sulphanilamide and sulphapyridine were in common use, many new sulphonamides are now available, of which the most generally useful are sulphathiazole, sulphadiazine and sulphamerazine for wound treatment and systemic administration (all much more potent than sulphanilamide and less toxic than sulphapyridine), and sulphaguanidine and succinyl-sulphathiazole for infections of the alimentary canal. Penicillin, discovered by Fleming in 1929, was purified and studied by a group working under Florey between 1940 and 1943, and is now being produced on a large scale by British and American manufacturers. The sulphonamides and penicillin have not abolished infection, for they can act only on bacteria which they can reach, and are therefore powerless against those

ying in abscess cavities or among dead tissues, but they can keep a local infection local and, with surgical help, can usually eradicate it. In traumatic surgery their prophylactic use has largely abolished cellulitis and systemic infection, and made wound excision safe and successful, even several days after injury. They have made the early closure of war wounds a routine procedure. They have allowed compound fractures to be converted into closed ones by suture, and enabled reconstructive operations to be performed in areas of recent infection without the danger of systemic flare up.

Chemotherapy is not as yet universally applicable, although the field of fire of the sulphonamides and penicillin overlap to some extent, there are still blind spots. Most of man's microbial enemies, those causing the acute infections and venereal disease, are sensitive to one or the other, usually to both. *Bacillus coli* is untouched by penicillin but arrested by sulphonamides, spirochaetes and staphylococci are penicillin-sensitive but sulphonamide-resistant. The tubercle bacillus and two organisms with a high nuisance value, proteus and pyocyaneus, resist the attacks of both. At the present time penicillin is preferred for the majority of infections when conditions allow laboratory control of its preparation and administration. The sulphonamides hold their place in most infections of the alimentary tract and as prophylactics in operations on the large intestines, and for other infections treated in the home or the wilds. Now that chemotherapy is an established fact it seems certain that drugs to attack the remaining immune bacteria will soon be discovered.

RENDERING PATIENTS SAFE FOR SURGERY

Estimation of bodily requirements—Advances in the treatment of shock and infection are two examples of a general progress in making patients safe for surgery. A general estimation of the patient's bodily needs, in blood constituents, in foodstuffs, in water, in salts, and in vitamins, is made before any major undertaking, and care is taken that reserves of each are fully charged before operation and that a correct balance is maintained afterwards. With the publication by Van Slyke of a simple copper sulphate method of estimating plasma proteins, the study of protein requirements has passed from the sphere of laboratory research to that of routine bedside investigation. The protein level, normally 6·7 per cent, drops when plasma is lost from the surface, as in wounds or burns, or when protein intake is low, as in starvation, invalid diet, and intravenous medication, and while it is low all metabolic processes, including those of repair, are handicapped. The level can be restored and maintained by a high protein diet, by infusions of plasma, concentrated if necessary and in extreme cases, when the mechanism of gastric digestion has been removed by surgery or damaged by starvation, by giving protein digests or amino-acids through a duodenal tube. Intravenous administration of amino-acids has not, as yet, proved entirely safe or satisfactory.

Hæmostatic agents—With patients better prepared, new technical devices and new materials have contributed to simplify some surgical procedures, or to make them more satisfactory. The power of fibrinogen to clot on the addition of thrombin or an extract containing it, has prompted its use as a hæmostatic and as a glue. Fibrin foam, a sponge-like preparation, has proved the most satisfactory hæmostatic in neuro-surgical operations, taking the place of Horsley's wax and muscle grafts; fibrin glue is used for nerve suture, particularly when the nerves concerned

are small and there is little tension at the joints, and also to fix split skin-graft to their bed. Fibrin is used in sheets to cover dural defects.

New technical devices—The control of infection provided by chemotherapy has encouraged a wider use of non-absorbable materials in surgery. Ligatures of fine silk, linen, cotton or nylon have replaced catgut in many clinics. Silk and nylon bid fair to oust fascia in the repair of large herniæ. New materials have been found that undergo no chemical change in the body, and are therefore received kindly by the tissues. Plastics have provided many of these new materials. Acrylic resin is widely used in prostheses to replace skull defects, and to a lesser extent in other parts of the skeleton. Flexible plastics are tending to supplant rubber and gutta serena for transfusion apparatus, gastric and duodenal tubes, and urethral and ureteric catheters and bougies, when their ability to withstand prolonged and repeated boiling and their freedom from flaking are advantageous. Absorbable plastics are undergoing trial. An absorbable cellulose-nitrate gauze promises to be of value in arresting oozing from deep sites, such as tears in the liver, since a pack of this material need not be removed. Absorbable plates and pegs are undergoing trial in bone surgery.

Two non-irritant metals, vitallium and tantalum, have been introduced within the past few years. Vitallium is an alloy, tantalum an element. Vitallium is light and reasonably cheap, but it cannot be bent or moulded, tantalum is heavy and expensive, but ductile. Vitallium is largely used in bone surgery, for plate screw and Smith-Petersen nails, and has even been used to replace missing pieces of the skeleton, such as the carpal scaphoid. Tantalum finds its chief employment in neurosurgery, as sheets in the immediate repair of skull defects, as wire in nerve suture, and as foil to wrap round nerve anastomoses.

Anæsthesia—In discussing the factors that have made for surgical progress, advances in the parallel field of anæsthesia must not be forgotten. It is not the place of a surgeon to discuss anæsthetics, but as a craftsman working on materials whose quality is entirely dependent upon the anæsthetists' ministrations, it is his duty to acknowledge the vast improvement that has taken place in their art within the past ten years, an improvement in the drugs employed, in the methods of their employment, and in the skill and standing of the anæsthetists themselves.

With modern anæsthesia, patients carefully prepared, improved technical devices, and new means to combat shock and sepsis, operative surgery has reached a new level of safety and achievement. Ten years ago the performance of such operations as total gastrectomy, resection of the œsophagus and pneumonectomy was a rarity, and recovery of the patient even more unusual. To-day, such operations are accepted as a matter of course in large clinics, and it is deaths that excite comment. Those who were fortunate enough to hear Major D. W. Harken of the United States Army report a series of 139 operations on the heart and thoracic blood vessels without one death, including fifteen operations on the heart, among which the same heart was opened on three occasions for a bullet that drifted from chamber to chamber and was recovered the third time, must have admitted that here was a new standard of achievement.

REGIONAL ADVANCES

A survey of advances in the different spheres of surgery can be no more than an inventory, and the choice of subjects for inclusion or omission must be haphazard.

Vascular surgery has benefited from the stimulus of war and a number of technical discoveries. Acute vascular injuries were studied at special centres in each of the main theatres of war, and the work was coordinated at three centres in Britain. The reparative surgery of arterial injuries has become a practical proposition with the use of heparin to suspend clotting. Heparin, the natural product, although still expensive and in short supply, is preferred to dicoumarol, the drug, which has proved unreliable and even dangerous. Arterial anastomosis has been simplified by the use of Blakemore's tubes, small vitallium cylinders through which a segment of vein is threaded and turned back as a cuff, the tube and vein are then plugged into the artery, like a glass connexion into rubber, giving an intima-to-intima junction without suture. In war injuries, tubes of glass or metal have been inserted to bridge the gap in a main artery, such as the femoral, and to maintain the distal supply until a collateral circulation has been established. Continuous heparinization is necessary to prevent clotting, and the method is therefore inapplicable when other injuries are present.

Much has been learned about the maintenance of nutrition after arterial interruption. The needs are to get blood to the distal areas, to make that blood carry the maximum of oxygen, and to reduce the call for oxygen of the starved tissues. Dilatation of collaterals may be encouraged by injection or resection of the sympathetic supply to the part, but an increased distal supply is probably obtained more effectively by the reflex stimulus of warmth. The vasomotor nerves are thought to be largely concerned with temperature regulation, that is, with the surface vessels, and the deep vessels to be under chemical control, if this be so, sympathetic denervation of a limb whose blood supply is barely sufficient, will starve the muscles by increasing the supply to the skin. In the late surgery of aneurysm, however, sympathectomy performed some time before operation will decrease the dangers of distal ischæmia when the affected segment is excised by preparing a by-pass of dilated surface vessels.

Full restoration of the blood picture by transfusion, so that blood arriving distally is fully charged with oxygen, is the second essential, keeping the threatened limb cool, but not cold, is the third. It has been shown that the demand of muscles for blood at 40°C is eighteen times that at 25°C . In a limb kept at the temperature of a cool room the metabolism is reduced to a level that the reduced blood supply can cope with, when the rest of the body is warmed at the same time the blood is sent through in maximum quantities. The principle of reducing the demands of the tissues by cooling to meet a reduced blood supply has also led to advance in the treatment of frostbite and of trench and immersion foot. Freezing the limb, or indeed reducing the temperature much below 20°C , is harmful.

In the study of arterial disease and of the late results of arterial and arterio-venous injuries, arteriography has been increasingly employed since perabrodil has been shown to be a safe and satisfactory contrast medium. In the surgery of veins there is a tendency to forestall thrombo-embolic disasters after abdominal operations by ligation of the superficial femoral vein below the point of entry of the saphenous and profunda branches in patients developing leg tenderness and infarcts. Chemical sclerosis of varicose veins is falling into increasing disrepute. The advance in *thoracic surgery* is beyond a brief review. In general, major operations, such as dissection pneumonectomy and resection of the œsophagus,

have been progressively perfected and rendered reasonably safe. The heart and the great vessels are attacked with increasing courage and a diminishing mortality. To the older interventions for the repair of injuries, the removal of foreign bodies and the resection of a constricting pericardium, has been added surgical attack on the patent ductus arteriosus, an operation carrying in practised hands a mortality no higher than that of appendicectomy in those of the occasional surgeon. The diaphragm is not the barrier between thoracic and abdominal surgery that it was a few years ago, but a door that may be opened from either side. It is becoming common to attack organs in its cupola from above rather than from below, and to bring the fundus of the stomach into the thorax for anastomosis in resections of the lower half of the œsophagus.

Abdominal surgery, having shown its maximum acceleration half a century ago has few opportunities for spectacular change, but the advance to increased safety has been none the less real. Most of the factors that have contributed are accessory rather than operative—the physiological outlook which has abolished the old drastic preparation and post-operative regime, the reasoned use of intravenous therapy, and gastric or intestinal suction, modern resuscitation and modern chemotherapy. The Fowler position, at any rate its routine employment, is in disfavour as predisposing to pulmonary collapse and thrombophlebitis, and early movement and even early ambulatory are increasingly supported.

In the surgery of abdominal wounds one principle alone, the exteriorization of colon injuries, is new in the present conflict, but the results are fully 100 per cent better than in the 1914-18 war, largely owing to the accessory methods mentioned above. In gastrectomy for chronic duodenal ulcer, prepyloric section with removal of the mucosa as far as the pylorus, has proved a valuable expedient when fisting and scarring make duodenal invagination unsafe. At the other end of the alimentary canal the performance of abdomino-perineal resection of the rectum by two surgeons working simultaneously, one in the abdomen and one in the perineum, has been found to halve the difficulties, the loss of blood, and the time needed for the operation, and to render it almost shockless. In hernia surgery there is much that is recent, but little that can be conscientiously included as an advance.

The general surgeon travelling along the high road is aware only of the main advances in *neurosurgery* and *orthopædics*, those large enough to rise above the hedges that surround these twin fields, or near enough to the border to cause boundary disputes between neighbouring cultivators. In this last category may be included the surgery of peripheral nerve injuries and of herniation of the nucleus pulposus. In peripheral nerve injuries the methods of examination, the technique of suture, and the prognosis are much as they were at the close of the 1914-18 war but certain improvements have appeared. Electro-myography enables the surgeon to determine the prospects of useful regeneration in a divided nerve at a much earlier date than is otherwise possible. It is now held that, after the first month the site of injury should be explored as soon as it can be established with reasonable certainty that recovery is not taking place. Fine tantalum wire is widely used as suture material, and fibrin glue for such procedures as the insertion of grafts or cable grafts where the gap is too wide for suture. Nerve grafts, although their use is backed by experimental surgery, have not as yet provided any instances of useful clinical recovery.

Herniation of the nucleus pulposus has been found to occur much more commonly than was realized at the time when it was first described by Mixter ten years ago, and neurological symptoms due to pressure from the protrusion have

described and relieved by operation at all levels of the spine. The modern operation is one of limited approach and radical removal: the affected disc is reached in the lumbar region through a trapdoor in the ligamentum subflavum without any removal of bone, and, after the protruding piece has been removed, the remaining soft portions of the nucleus are removed by curettage.

In the surgery of cranial injuries, attention has been focused on the prevalence of late infections after wounds of the base involving the air sinuses. To guard against this complication the dural perforation in the cranial floor is sealed by a transplanted fascial flap, either at the primary operation, or as soon after healing as an aseptic field can be secured. In theatres of war, maxillo-facial surgeons are now teamed with neurosurgical units, largely with the treatment of this type of case in view. Neurosurgery has recently come to the aid of psychiatry with the operation of pre-frontal leucotomy. After division of the association fibres from the pre-frontal region of the brain, an emotional, unstable and occasionally maniacal patient is transformed into an unambitious and unimaginative but useful and reliable citizen. In published series the death rate is only 2 per cent, and about 50 per cent of the patients have left asylums for remunerative employment, whilst others can be safely cared for at home.

The war has brought two changes in *fracture surgery*. Stress fractures, apart from march fracture of the second or third metatarsals, were almost unknown, except in German literature, five years ago; to-day they are a commonplace at any hospital or sickroom serving a centre where young men or women are in training. The reasons are, first, a real increase due to the number of youths subjected to unaccustomed physical strain, second, recognition of the real nature of symptoms that were formerly dismissed as "rheumatic", owing to improved facilities for radiography. Stress fractures are chiefly found in the lower limb, in the metatarsals, the os calcis, both ends of the fibula, the upper end of the tibia, the shaft and the neck of the femur; they repair rapidly with relief of strain.

The second change is a greatly increased use of internal fixation by plates, screws or wires. This revival of the operative treatment of fractures is largely the result of the increased protection against infection given by the sulphonamides and penicillin. Internal fixation has been widely practised by forward surgeons in the treatment of gunshot fractures of the long bones, but the reports now coming in from base areas, and especially from America, indicate that open fractures so fixed give trouble later in about 40 per cent of cases. In closed fractures, however, the method, which is a return to the teaching of Lane forty years ago, offers a means to attain the ideal result, perfect anatomical restoration of the bone and perfect functional recovery of the joints.

The ill wind of war has blown good to surgery and surgeons, and, through them, to coming generations. The young men of the Services who have been fortunate in their opportunities and made the most of them, who have been well advised and supervised and given the needed alternation between base and forward work, bring back to civil life a new standard that augurs well for future advance.

CHEMOTHERAPY

By SIR LIONEL WHITBY, CVO, MC, MD, FRCP

Regius Professor of Physic, University of Cambridge

IN the field of chemotherapy, during the past year, the advances have been of the nature of consolidation rather than of spectacular new discoveries. There is now a better understanding of the scope, limitations and dangers associated with drugs of the sulphonamide group, whilst certain new compounds have been developed which have some advantages over the well-tried favourites. The value of penicillin has been assessed and properly appreciated, its production and stability have been improved, and, with more generous supplies available, its use in a number of diseases has been explored. At the same time, the potentialities of numerous other products of moulds and bacteria have been systematically investigated, although none has reached the stage of general use and none has yet been found which can compare in potency and everyday utility with penicillin.

SULPHONAMIDE GROUP

There is a general belief on theoretical grounds, supported to some extent by experimental evidence, that the maximum bacteriostatic activity of a sulphonamide is represented by sulphadiazine and that no compound more highly active will be discovered. This, however, does not mean that new derivatives may not be found which have a higher ratio of therapeutic activity as compared with toxicity.

The well-known compounds for the treatment of common coccal and coliform infections include sulphanilamide, sulphapyridine, sulphathiazole, and the less easily obtained sulphadiazine. To these have been added sulphamezathine and sulphamerazine, both of which are variants of sulphadiazine. All these drugs, with limitations in the case of sulphanilamide, are largely interchangeable, but there are certain circumstances in which one or the other is preferable, and some special advantages are claimed for the two newer variants. Sulphanilamide is used only in streptococcal, gonococcal, meningococcal and coliform infections; for the latter, in the urinary tract, sulphanilamide is still the best routine drug because there is no danger of crystal formation. Either sulphapyridine, sulphathiazole or sulphadiazine is required in pneumococcal infections, whereas, although the last two are the best of the group for staphylococcal diseases, they are in no way comparable in effectiveness with penicillin. For routine use, either sulphathiazole or sulphadiazine are the most favoured, mainly because they cause less side-effect than sulphapyridine. Yet with the latter, excellent results can be obtained and the most troublesome complication, vomiting, can be largely eliminated by dividing the doses into small portions at frequent intervals. The only real advantage which sulphadiazine possesses over sulphathiazole is that its pharmacology permits it to be administered six-hourly, instead of four-hourly. With sulphapyridine, sulphathiazole and sulphadiazine, there is always a danger of urinary trouble.

less fluid intake and output are adequate and the urine not highly acid. This is because the acetylated crystals of these three compounds are insoluble in an acid or a concentrated urine. An intake of at least three litres with an output of at least one and a half is an integral and important part of treatment when these drugs are used.

Sulphamezathine, from the theoretical aspect, as well as from practical experience, does not lead to crystal formation in the urine. For this reason alone, the drug can be considered to be a real advance, more especially as its therapeutic activity is of the same order as the parent compound, *sulphadiazine*. The drug will undoubtedly find a great use with the fighting forces in tropical climates, where the problems of dehydration and fluid balance render the use of the crystal-forming drugs a hazardous procedure. Rose, Martin and Bevan (1943) describe the pharmacological and antibacterial properties of *sulphamezathine* as compared with *sulphanilamide* and *sulphapyridine*. On oral administration in equal dosage, the blood level of *sulphamezathine* reached a higher maximum than with either of the others, the maximum being attained slightly later than with *sulphanilamide*, and considerably earlier than with *sulphapyridine*. Furthermore, the curve of the blood level was continuously above that of *sulphanilamide*, thus showing that the excretion rate was slower. Generally speaking, it may be said that *sulphamezathine* resembles its parent *sulphadiazine*, it is readily absorbed and slowly excreted, thus permitting maintenance of a relatively high blood concentration with doses smaller or less frequent than with most other members of the group. No serious toxic effects have been observed in man, and the risk of renal damage is less with it than with any other sulphonamide except *sulphanilamide*. This last feature makes *sulphamezathine* an appropriate drug for treating genito-urinary infections.

Sulphamerazine closely resembles *sulphadiazine* in its general action and pharmacology, but it is more readily absorbed than the parent substance, so that smaller and less frequent doses are needed to keep up suitable drug levels in the blood. Hall and Spink (1943) give an account of its clinical use and claim that it is at least no more toxic than *sulphadiazine*, that it causes less nausea and vomiting than *sulphapyridine* and that fewer cases of drug fever or skin rashes were seen than would have been expected with *sulphathiazole*. From the different accounts, it is fair to conclude that *sulphamerazine* is an alternative to *sulphadiazine*, but that it has no far-reaching advantages over the latter.

LOCAL APPLICATION—A local application of a sulphonamide has proved of considerable value in the treatment of certain skin infections. As would be expected, the results are satisfactory only when the infection is due to a susceptible organism, such as the β -haemolytic streptococcus or staphylococcus, and this demands considerable experience and skill in differentiating a susceptible condition, such as true impetigo, from the many other impetiginized lesions which may be found in practice. *Sulphathiazole* is the drug of choice, and should be applied night and morning in a concentration of 5 per cent in a cream or paste, as such, it should cure the majority of cases within a week (Peterkin and Jones, 1943). It should be borne in mind that sensitization to *sulphathiazole* or to light may follow the application of the drug to the skin, especially if the treatment be continued for more than seven days.

The sulphonamides have been extensively used for application to wounds or to serous cavities, with a view to preventing or treating infection. General experience suggests that although the practice may be advantageous as a single application *ab initio*, there is little point in making repeated applications, in that the same concentrations can be obtained in any inflammatory or serous exudate by means of oral administration. It is well known that local applications are valueless where pus formation is free, but there is one sulphonamide—*marfanil*—which is said to be active even in the presence of pus, it is unsuitable for oral administration. In general, sulphanilamide, being the most soluble, is perforce the most suitable drug for local application. A mixture of sulphathiazole powder (1 part) with sulphanilamide powder (3 parts) will, however, maintain a high local concentration for a longer time. Sulphathiazole and sulphadiazine have also been prepared as microcrystalline suspensions (15 to 20 per cent) which have been favourably reported upon for local use.

INTESTINAL INFECTIONS—For many years, sulphaguanidine has held pride of place as the best sulphonamide for the treatment of the acute bacillary dysenteries. This preference has been based on the view that the drug can be taken in a large dose with little absorption, so that a high and effective concentration remains in the gut to exert a beneficial action. It is now known, however, that although absorption is slow, nevertheless the amount absorbed, and afterwards excreted by the kidneys may be something more than half the total dose administered. The low blood levels are due to the slow absorption and relatively rapid renal excretion which may be associated with urolith formation. The modern view is that equally good results can be obtained with the routine doses of sulphapyridine, sulphathiazole or sulphadiazine, following a course of treatment with which most of the profession is familiar. Succinyl sulphathiazole, a variant of sulphathiazole, has also been favourably reported upon for the acute bacillary dysenteries, for the carrier state and for reducing the numbers of intestinal organisms before operative procedures on the intestine, it is said to be more effective than sulphaguanidine in the Sonne type of dysentery.

PENICILLIN

For long, the supplies of penicillin were so restricted that its use was confined to the treatment of infection or diseases occurring among the fighting services. This was, in many ways, a blessing, in that the scope, limitations and the factors important for successful treatment were fully assessed by competent observers. Now that the product is more freely available, it is essential that the lessons of the experience should be widely known. The scope of penicillin is limited to infection with gram-positive bacteria, more especially *Staphylococcus aureus* and *albus* (against which it is the most potent remedy known), *Streptococcus pyogenes*, some pathogenic strains of *Streptococcus viridans*, pneumococcus, *Corynebacterium diphtheriae*, Clostridia, *Treponema pallidum* and probably the spirochaetes of relapsing fever and Weil's disease. Gonococcus and meningococcus are also highly susceptible, but almost all other gram-negative organisms, especially *Ps. pyocyaneus*, *Proteus vulgaris* and the coliform group, are quite unaffected.

Modes of administration and dosage—At the present time, penicillin is used in the form of tablets of the sodium and calcium salt, each tablet being standardized to contain 10,000 to 15,000 units of penicillin. In actual fact, not more than about 10 per cent. of the tablet consists of pure penicillin, the remainder being impurities to which the rare reactions are attributed. The effective single dose for an adult is about 15,000 units, which will maintain a bacteriostatic concentration in the blood for a period of about three hours, after which time the dose must be repeated. Owing to complete lack of toxicity, much larger doses may be given with perfect safety. Penicillin can be applied locally, especially to special sites such as the eye, but it is mainly used by parenteral injection, it cannot be given by mouth. The injection may be made subcutaneously, intramuscularly or intravenously by whichever route it is given, the dose must be repeated every two to three hours or else arrangements made for continuous infusion. When the intravenous route is employed, thrombosis is a common complication. Hence, the other two routes are more commonly used. In due course, there is no doubt that some method will be devised whereby a "depot dose" can be injected which will ensure steady absorption over a long period of time. Some success has already been attained in this direction by Romansky and Rittman (1944), who claim that with suspensions of calcium penicillin in beeswax and peanut oil, an effective concentration is maintained for seven to ten hours after a single injection, others have claimed that the application of an ice-bag to the site of injection leads to a slow and continuous absorption. The trials which have been made with penicillin in the treatment of gonorrhœa and syphilis provide a promising prospect for the early cure of these disabling diseases. Nevertheless, it may be many years before the final assessment can be made in the case of syphilis, for there is always the bogey of suppression, rather than eradication, leading to the development of tertiary disease in the distant future. With gonorrhœa, the intramuscular injection of 20,000 units three-hourly for a period of twenty to twenty-four hours appears to cure the disease completely in the majority of cases, even though they be sulphonamide-resistant (Ferguson and Buchholtz, 1944, Robinson, 1944). There is also evidence that sulphonamides enhance the activity of penicillin in gonorrhœa.

Syphilis appears to require the intramuscular injection of at least 20,000 units three-hourly, night and day, to a total of sixty injections, occupying a period of seven-and-a-half days (Moore, *et al*, 1944). Even so, the relapse rate is considerable, and the recommended dose has now been doubled to 2,400,000 units in seven-and-a-half days. Much remains to be done in purifying penicillin and improving the mode of administration. It should be appreciated that the meninges and serous membranes form a barrier across which penicillin does not readily pass. Infections of the theca, of the serous cavities and of joints should therefore be treated by direct injection.

Maintenance of potency—Finally, it is necessary to be fully aware of the factors which destroy penicillin or reduce its activity. Although highly active in pus (in contrast to the sulphonamides) penicillin is rapidly destroyed by acids and alkalis (it is only stable between pH5 and pH7), by heat (e.g., it cannot be sterilized by boiling or autoclaving), by heavy metals (copper, mercury, lead), by alcohols (e.g. spirit), by oxidizing agents (e.g. hydrogen peroxide and potassium

permanganate) and by enzymes produced by many common aerial bacteria as well as coliform bacilli. Furthermore, although the dry tablets are stable, particularly at refrigerator temperature, they are extremely hygroscopic, they rapidly deteriorate if allowed to get damp, and once they are made into solution, the latter quickly loses its potency. From these facts, one or two practical points emerge. Solutions must be freshly made under completely sterile conditions. Reservoirs which contain material for infusion must have an air filter on the inlet, to avoid aerial contamination. Glass and rubber tubing must be of such a quality that they do not, by reaction or by impurities, exert a deleterious action on the material. This is especially so in the case of rubber tubing, which should preferably be of finest Latex quality, war-time synthetic rubber tubing rapidly destroys penicillin.

OTHER MOULD AND BACTERIAL DERIVATIVES

The success attending the exploitation of penicillin has naturally led to a thorough search for antibiotic substances derived from other moulds or from bacteria. On the whole, success has been limited, for although a number of potent substances have been found, nearly all have been too toxic for human use, and none has shown a power at all equal to penicillin. The main interest lies in the fact that some of these antibiotics are active against gram-negative bacteria, thereby being complementary to penicillin, they give a clear indication that the potentialities of the field are by no means exhausted. Mould derivatives have included *Citrinin* from *P. citrinum* (active against gram-positive bacteria), *Spinulosin* from *P. spinulosum*, *Fumigatin* from *A. fumigatus* and *Patulin* from *P. patulum*. All of these substances are of relatively simple structure, and some have been synthesized. Patulin enjoyed a meteoric career as a cure for the common cold, but the claim has since been shown to be unfounded.

The most promising new materials have been obtained not from moulds, but from soil actinomycetes and soil bacteria. The most interesting has been an autolysed culture of a soil bacterium *B. brevis*, first identified by Dubos (1939), which has been found to contain two different crystalline bodies known as *gramicidin* and *tyrocidin*, the former is active against gram-positive organisms and the latter against both gram-negative and gram-positive organisms. Both substances are toxic when administered by parenteral routes, and such clinical trials as have been reported have been concerned with local application only. More recently a different strain of *B. brevis* has been investigated by Russian workers who claim to have extracted a material known as Soviet gramicidin or gramicidin S which, when applied locally in experimental animals, is capable of preventing the development of gas-gangrene (Gause and Brazhnikova, 1944).

Antibiotics from soil actinomycetes have revealed an even more promising prospect. Thus, Schatz *et al.* (1944) and Waksman *et al.* (1944) have described *Streptothricin* and *Streptomycin*, the latter obtained from *Actinomyces griseus*. Streptothricin is highly stable, resists moderate heat, can be stored, and is unaffected by the enzymes of other bacteria. It inhibits the growth *in vitro* of *B. subtilis*, *B. coli*, *Staphylococcus aureus*, *Brucella abortus* and a number of gram-negative organisms, including those belonging to the proteus, pseudomonas,

- *Shigella* and dysentery groups. It has also an inhibiting action on the tubercle bacillus and may therefore prove to be the starting point for an effective attack on this disease. Its toxicity for animals is low.

TUBERCULOSIS

With the advent of each new chemotherapeutic substance there is always the hope that it may be effective in treating this widespread and mortal disease. The alphonamides and penicillin have proved useless. But there are indications that the problem may sooner or later be solved, either by a single remedy or by a combination of the widely differing materials which have been found to have some inhibitory action on the tubercle bacillus. In 1940, Findlay concluded that none of the remedies to date, including the salts of heavy metals, had been shown to have a decisive influence on the course of the human infection. Henshaw and Feldman (1941) opened a new prospect with their work on sulphones, of which one, known under the trade names of promin and promanide, justified clinical trial. The results were disappointing. The latest example of *in vitro* bactericidal action against the tubercle bacillus is the claim that diethyl stilbæstrol is effective (Faulkner, 1944). This most interesting observation may perhaps be correlated with the well-known clinical finding that tuberculous women appear to improve in health during pregnancy. Finally, there is the discovery recorded above concerning the action of streptothricin upon the tubercle bacillus. None of these findings has in any sense entered the realm of practical medicine, but it is clear that light is being shed on the universal problem of tuberculosis from many different angles, and there is some indication that coordinated work in the post-war years may provide a happy solution.

References

- Dubos, R. J. (1939) *Proc Soc exp Biol Med*, 40, 311
 Faulkner, G. H. (1944) *Amer rev Tuberc*, 50, 167
 Ferguson, C., and Buchholtz, M. (1944) *J Amer med Ass*, 125, 22
 Findlay, G. M. (1940) *Ind med Gaz*, 75, 632
 Gause, G. F., and Brazhnikova, M. G. (1944) *Lancet*, 2, 715
 Hall, W. H., and Spink, W. W. (1943) *J Amer med Ass*, 123, 125
 Henshaw, H. C., and Feldman, W. H. (1941) *Ibid*, 117, 1066
 Moore, J. E., et al (1944) *Ibid*, 126, 67
 Peterkin, G. A. G., and Jones, E. C. (1943) *Brit med J*, 1, 318
 Robinson, J. N. (1944) *Brit J Surg*, 32, 211
 Romansky, M. J., and Rittman, G. E. (1944) *Bull U S Army med Dept*, No 81, p 43
 Rose, F. L., Martin, A. R., and Bevan, H. G. L. (1943) *J Pharmacol*, 77, 127
 Schatz, A., Bugie, E., and Waksman, S. A. (1944) *Proc Soc exp Biol Med*, 55, 66
 Waksman, S. A., Bugie, E., and Schatz, A. (1944) *Proc Soc exp Biol Med*, 55, 537

tinplate industry Vernon (1919) found that without artificial ventilation the output of the metal-rolling teams was 12 per cent less in the summer months than in winter, but when they had good ventilation from fans revolving overhead, the summer output was only 3 per cent less than in winter. Accident liability increased by exposure to unduly high or low temperatures. Osborne and Vernon (1922) found that munition workers had the lowest number of accidents at an air temperature of 67° F. The accident rate rose at the lower and higher temperatures. At 52° F it was 35 per cent, and at 77° F 23 per cent higher than at 67° F. Vernon, Bedford and Warner (1928) also showed that a much greater number of accidents occurred in deep and hot mines than in shallower and cooler ones. The industrial medical officer should be constantly concerned with method of ventilating and heating workrooms. He should know how to measure warmth and air movement, and also the requirements for comfort in different types of work. The whole subject has been reviewed in detail by Bedford (1944).

VOCATIONAL PSYCHOLOGY

Vocational psychology includes vocational selection, which aims at finding the right person for the job, and vocational guidance, which attempts to discover the right job for the individual. The main task in vocational psychology is to devise tests which measure intelligence and special abilities, such as mechanical aptitude, and to determine the significance of these in the performance of various tasks. Such methods supply only part of the information required for fitting the square pegs into the square holes. Intelligence tests and sensori-motor tests have been shown to have a predictive value for skilled occupations. When the predictive value of these tests was compared with the results of entrance examinations of 1,130 aircraft apprentices, performance in the psychological tests was more closely related to subsequent proficiency than performance in the entrance examination (Farmer and Chambers, 1929). The value of psychological tests depends upon how they are applied to industry. If used for allocation rather than for rejection of the less fit and less intelligent workers, their scope will be enormous.

Vocational psychology should be aimed at detecting the capacity of children at an early age, so that they can be guided to careers offering *them* the best opportunity of success, rather than selecting them for jobs in the interests of the employers' output.

The Medical Research Council has lately established in the University of Cambridge a Unit for Research in Applied Psychology. Many of the investigations to be undertaken here will lie within the industrial field.

PREVENTION OF INJURY

It is admitted that medical officers in industry have not paid sufficient attention to the prevention of accidents. However well machinery may be guarded by law, not more than a 10 per cent reduction in the accident rate can be looked for by the provision of safeguards alone.

In Great Britain, Farmer and Chambers (1926, 1929, 1939) and Farmer, Chambers and Kirk (1933), have for many years been investigating the condition

of *accident-proneness* with a view to finding some test or tests which would serve as a means of identifying the affected persons in groups of industrial workers. They found that the probable number of such persons ranges from 10 to about 25 per cent. of the total. In order to obtain reliable information, they chose large groups of subjects whose age and experience were similar and of whom adequate accident records could be obtained for a number of years. In these subjects they established the fact that, with equal exposure to risk, roughly three-quarters of recorded accidents happened to one-quarter of the people exposed. Unfortunately, few firms subject their new employees to psychological tests before assigning them to one occupation or another. But in the absence of such tests it would be possible to sift them roughly by putting them for a time on occupations free from major risks, and only after they have shown themselves to be reasonably free from accident-proneness to transfer them to more dangerous occupations. Accident-proneness is greatly influenced by the mental attitude of the subjects. The accident-prone are apt to be insubordinate, temperamentally excitable and to show a tendency to get flustered in an emergency. These and other defects of personality indicate a lack of aptitude on the part of the subjects for their occupation (Vernon, 1945).

To-day, the medical officer in industry deals with accidents largely from the point of view of providing first-aid treatment for major injuries, and continuous treatment in the case of minor injuries. Lately, a few industries have made a forward step in assisting injured workmen to regain full function after injury by providing rehabilitation shops and special centres. All these are important aspects of the industrial medical officer's work, particularly in the heavy trades where the severity and frequency of accidents are high.

Protection of the eyes—In many trades the eyes need special protection against accident, and this is best secured by a goggles programme within the factory. The safety engineer must enlist the interest of all workers exposed to risk. In a plant employing two thousand people or more, it is advisable to have a full-time, specially trained goggles man. His job is to dispense, adjust and repair industrial goggles, and it is essential that he should patrol all workshops regularly, covering the entire plant as often as is necessary. In many large factories in the U.S.A. the goggles service man is in a distinctive uniform, and uses a push-cart brightly painted and decorated with slogans (Kuhn, 1944). Men and women working long hours will not, and cannot, wear goggles that hurt or that do not fit. By adjusting a spectacle frame which is causing discomfort, or by replacing a pitted lens, the service man not only helps the worker, but also enlists his goodwill, thereby ensuring the success of the entire programme.

SICKNESS RECORDS

Before 1939, many of the more enlightened organizations in Great Britain adopted their own method for recording sickness absence. They realized that such records would not only help them to determine the effective labour strength, as opposed to the book strength, of their staff, but would also enable them to keep a check on the effect of conditions of work on the health of those employed in the various departments of the factory, shop or office. Methods adopted were, however,

evolved separately in each firm, and could not be used for comparing the sick rates of different firms. They lacked uniformity, which is essential for a statistical comparison. A report of the Industrial Health Research Board (1944) recommends the use of an individual record card or, as an alternative, a register or nominal roll of sickness absence. The record card is designed to deal with the history of a case over two years. The report suggests that it is cheaper to classify certified sickness only, and seven classes are proposed: influenza and other respiratory disease, digestive disease, rheumatism, functional nervous disorders, accidents at work, and unclassified conditions. If such a scheme is to be really effective it must be developed on a comprehensive or national basis. Only thus is it possible to compare the health, and therefore possibly the occupational factors affecting health, of quarrymen in Buxton with that of railway porters at Paddington or dockers at Liverpool with workers in the engineering trades of Coventry. A possible clue to causation can be obtained in this way and preventive and remedial measures sought and research initiated. Thus social biology can be linked with industrial medicine.

WOUND INFECTION AND BURNS

Prevention of sepsis—The treatment of minor injuries occurring at the place of work is an important part of the work of the industrial medical officer and nurses. The higher the standard of treatment in the factory the less is the risk of sepsis, with its consequent absence from work and increase in permanent disability. Even to-day most workpeople have no nurses or medical officers to supervise the treatment of accidents. In many instances the diagnosis of "sepsis" is left to the first-aid worker and the untrained nurse, and often to a welfare supervisor or an office clerk. At the Birmingham Accident Hospital the bacteriology unit of the Medical Research Council is studying wound infection as it affects industry, and the work is being done in conjunction with physicians skilled in accident treatment, industrial medical officers and nurses. Gissane, Miles and Williams (1944) claim that many wounds are already septic when first seen in the factory surgery, and that a proportion of open wounds become septic during treatment. "Silent infection", which may be present in up to 40 per cent of wounds treated at the factory, not only delays healing but also forms a reservoir of organisms capable of infecting clean wounds treated in the same surgery. The important point is made that an aseptic technique must therefore be designed to prevent cross-infection from those wounds already septic or "silently" infected. The difficulty of altering present conditions, and of instituting an aseptic technique is recognized, but the first stage in this direction is the proper planning and layout of the industrial dressing station. Without this a suitable technique cannot be established, nor infection controlled.

First-aid treatment of burns—Another contribution of much interest to industrial medical officers is that of Colebrook, Gibson and Todd (1944) on the first-aid treatment of burns. In certain industries, for example the casting of metal, burns are only too common, and the wastage of man-hours from this cause is well recognized. But most burns in industry are not serious enough to need hospital treatment, yet no matter how trivial, every burn is a source of infection. The

authors maintain that it is important to distinguish clearly between temporary treatment at the scene of the accident, or first-aid, and the further treatment carried out by a medical officer or nurse, which they term *plenary* treatment, to convey the idea of completeness. The treatment of burns is intimately bound up with the problems of wound infection, and the main conclusion which Colebrook comes to is, that avoidance of infection by the hæmolytic streptococcus should dominate first-aid policy for all but very severe burns, for which general measures often have to take precedence over local treatment. A simple first-aid measure is recommended, namely the local use of a water-soluble cream containing 1 per cent. of cetyl trimethyl ammonium bromide and 3 per cent. sulphanilamide. Part of the experimental work has been done within the factory dressing station as well as the hospital, and the arguments in favour of giving an extended clinical trial to this new method are convincing.

OCCUPATIONAL DERMATITIS

The early diagnosis of occupational dermatitis is of the utmost importance, so that the employed may be removed from contact with the causative agent. Any other course may lead to intractable skin disease associated with sensitivity to many agents. The expansion of medical services in industry during the 1939-45 war, has led to more adequate supervision of factory personnel. Selection of employees by pre-employment examinations, frequent medical inspections and prompt first-aid treatment are measures of importance in reducing the incidence of occupational dermatitis. Employees and supervisors should be instructed in the nature of the hazards encountered during work, in clean methods of work, and how to take care of the skin. Increasing attention to factory hygiene, and particularly to plant design, are of vital importance so as to reduce the chances of irritant materials coming in contact with the skin.

Measures of prevention—Provision of protective clothing, and carefully chosen barrier creams are important but less satisfactory preventive measures and, although they are often necessary, they should not be relied upon by themselves unless it is impossible to reduce the hazard by improvement of plant design. Adequate washing facilities are essential in factories where irritant materials are used, and it is necessary to stress their strict supervision when once provided. The correct application of barrier substances and the institution of washing facilities make it possible to eliminate irritant cleansing agents which often themselves cause skin disease.

In the *treatment* of the disease, early removal from contact with the irritant substance and protection of the inflamed skin are cardinal principles. The benefits of rest and hospital treatment for severe cases are striking. It is wise to seek the opinion of an experienced dermatologist at an early stage in severe or doubtful cases. In some cases X-irradiation is a most valuable therapeutic agent. The whole subject of occupational dermatitis has been reviewed by Jones (1945).

INDUSTRIAL TOXICOLOGY

(1) *METALS AND METALLIC COMPOUNDS*—The toxicology of inorganic substances has been reviewed by Farhall (1945). Metallic poisons have different

ready dressed The seed merchant must dress the seed in a completely closed paratus

In the case of *chromium compounds*, toxicity is determined by the valency of the metal radicle Chromium plating exposes the worker to spray which is carried to the air by bubbles bursting over the plating rack Hexavalent chromium compounds are used, and they attack the skin through the slightest abrasion, causing dermatitis and the well-known chrome holes or chrome ulcers In addition, perforation of the nasal septum occurs in more than half of the men exposed his toxic action is confined to compounds of hexavalent chromium Trivalent chromium salts, such as the phosphate and carbonate, have no toxic action (Katsuka and Fairhall, 1934) Whereas the popular demand for chromium-plated articles has given rise to much occupational ill-health, a new and harmless process is now being devised

The new Warner (1944) method uses trivalent chromium salts which not only promise to revolutionize chromium plating itself in a technical sense, but, since the salts are non-toxic, would eliminate the chromic acid hazard A new source of chromate exposure was recently shown by Greenberg and his associates (1942) to occur in connexion with spray painting In a survey of 106 painters in a large aircraft factory in New York State several cases of perforated septum were found which were attributed to the large amount of zinc chromate pigment present in the paint

In the development of *new alloys* many metals, rare or unknown a few years ago, are now assuming commercial importance So far no toxic effect has been discovered in workers handling cerium, gallium, indium, molybdenum, rhenium, titanium, tungsten and zirconium On the contrary, toxic effects are already known in the case of beryllium, cadmium, platinum, selenium, tellurium, thallium, uranium and vanadium Of these beryllium, cadmium, platinum and vanadium affect the respiratory system and will be considered later Workers exposed to selenium and tellurium are liable to exhale in the breath organic selenides and tellurides which have an astoundingly fetid odour In general, the toxicity of selenium has been exaggerated Dudley (1938) has reported pallor, gastrointestinal disturbances, garlicky breath and nervousness in men engaged in extracting or purifying selenium The toxicity of hydrogen selenide is high and the use of this substance requires careful control in industry It may produce intolerable irritation of the eyes and nose (Dudley, 1941)

Uranium and its salts are highly toxic Numerous studies of uranium nephritis in animals have been made since Leconte (1854) first showed that absorption of small amounts over long periods of time caused chronic nephritis MacNider (1936) has shown that in dogs poisoned with uranium, hepatic degeneration occurs, although sometimes the animal can repair the hepatic injury Dogs receiving sodium citrate can survive an otherwise lethal dose of uranyl nitrate, because such treatment facilitates the excretion of uranium in the urine (Gustafson, Koletsky and Free, 1944) Uranium poisoning in man is rare Workers handling it must be under constant supervision and, since it is a radio-active element, repeated blood counts must be taken If a worker excretes uranium in the urine it can be detected in extremely minute amounts

(2) *COAL-TAR COMPOUNDS* —The toxicology of industrial organic solvents

has been reviewed by Browning (1937) and of organic compounds in general by Hunter (1944). The coal-tar derivatives are so numerous and complex that it is difficult for the toxicologist to keep pace with the chemists who produce them. It is sometimes possible to predict from the chemical composition of the more simple members of this group what their physiological action is likely to be. Addition of a *nitro*- or *nitroso*-group usually produces a more toxic compound but it does not follow that toxicity will continue to increase as more *nitro*-groups are added. Thus 2-4-dinitrophenol is toxic, whereas trinitrophenol is practically harmless. The position of the substituent groups in the benzene ring may have an effect on the toxic action. Thus the toxic properties of 2-4-dinitrophenol are not shared by any of the other isomers. When a *nitro*-compound is reduced to an amine, as when nitrobenzene is reduced to aniline or nitrotoluene to a toluidine the toxic character remains much the same, but the intensity of the action is lessened. Sulphonation renders a compound non-toxic, as soon as aniline is sulphonated, it ceases to give trouble (Hamilton, 1925). But there is no inflexible rule for judging the toxicity of isomers. When the substituent group is in the *para*-position the compound is likely to be more toxic than the corresponding *ortho*- or *meta*-isomer (Fränkel, 1912). This is true of *para*-phenylenediamine, but in the case of tri-cresyl phosphate the *ortho*-isomer is the toxic one, and *meta*-nitraniline is more poisonous than *para*-nitraniline. Toxic activity depends not only upon chemical constitution, but also upon physical properties. It may be that toluene is harmless compared to benzene merely because of its higher boiling point and lower vapour pressure.

Benzene poisoning has been carefully controlled in Great Britain by the Factory Department of the Ministry of Labour. Special legislative requirements regarding ventilation of shops where benzene is used are laid down, and there is an important general requirement in the same connexion in Section 47 of the Factories Act, 1937. Legislation may also demand frequent examination of employees by the examining surgeon. Chronic benzene poisoning is notifiable as such and as toxic anaemia, so the chances of a case escaping notice are small. These protective arrangements are so satisfactory that in the ten years preceding the 1939-45 war only nine cases of chronic benzene poisoning were notified. Santesson (1897) and later Selling (1910) established the conception that benzene produced a toxic effect on the bone marrow, first destroying the platelets, then the granular leucocytes, and finally producing the complete picture of aplastic anaemia. Recently, however, largely owing to the work of F. T. Hunter (1939), it has been realized that the blood picture may vary from severe hypoplasia to the most extreme hyperplasia and even leukaemia. Hyperplastic reactions are more common in males and are found in patients only after prolonged exposure, hypoplasia, on the other hand, is more common in females and may follow either short or long absorption.

The outbreak of war in 1939, with the huge demand for aircraft and diversion of toluene to the manufacture of explosives, necessitated a slight relaxation of the high standard of protection against benzene and, as a result, anxiety was felt that some of the "dope girls" might show signs of intoxication. An excessive investigation was therefore carried out involving nearly 1,200 workers in sixteen factories (Hunter, Milton, Perry, Barrie, Loutit and Marshall, 1944). The workers, most

of whom were women, were exposed to low concentrations of benzene vapour. It was found impossible to detect any significant changes in the blood or any change in the inorganic total sulphate ratio in the urine of the groups of workers examined. Much work in the past has attributed leucopenia in such groups of workers to benzene poisoning, but this latest investigation shows that there is no justification for doing so, unless it is proved that the workers were in fact exposed to a toxic concentration of benzene in the atmosphere. In the "dope shops" examined it was found that the concentration in the general shop rarely rose above 10 parts per million, and even on such specialized jobs as spraying the insides of cockpits the concentration rose only to 45 parts per million, and then only for short periods of time. The toxic level for benzene in the atmosphere is usually stated to be 70-100 parts per million, but when the possibility of idiosyncrasy is considered, the only level which can be regarded as safe is zero. The situation with regard to benzene in Great Britain during the 1939-45 war may therefore be looked upon with satisfaction and pride. It is most unlikely that any "dope girl" has been poisoned with this substance, and it is difficult to find anybody who has been exposed to toxic levels. The Factory Department are to be congratulated on the way in which they have protected the worker from this hazard.

Tri-*ortho*-cresyl phosphate is used as an agent in the plastics industry to render the materials more pliable. It is known to be toxic and has been responsible in the past for several outbreaks of paralysis with bilateral foot- and wrist-drop. In 1930, an extensive outbreak occurred in the U.S.A. from drinking jamaica ginger (jake) which had been adulterated with this substance. Another outbreak was due to apioi, used as an abortifacient, which was similarly adulterated. Yet a third was caused by adulterated soya bean oil. Hunter, Perry and Evans (1944) reported the first cases of industrial origin.

These occurred in three men employed in the manufacture of tri-*ortho*-cresyl phosphate as a plasticizer. They had been at work for six to eight months at wash-tanks into which the phosphate was introduced at about 60° C, and, although it was immediately cooled, it was possible for the men to inhale the vapour, but it may have been absorbed through the skin. The toxic condition started with cramp-like pains in the hands and feet, difficulty in walking and attacks of diarrhoea. The picture was that of a polyneuritis with flaccid paralysis of the distal muscles of the upper and lower extremities. Complete recovery took place slowly, after some twelve months or so. A number of animal experiments have established that this substance is toxic when swallowed or absorbed through the skin, new experiments are reported in which the drug was given orally to fowls and caused paralysis. When preventive measures, particularly by adequate ventilation, were adopted at the factory concerned, no further cases occurred.

(3) **HALOGENATED HYDROCARBONS**—The entrance of chlorine into an aliphatic hydrocarbon increases its toxicity, whereas the reverse is the case with an aromatic hydrocarbon. Thus chlorobenzene is less toxic than benzene and causes no trouble in industry. The toxic effects of the chlorinated hydrocarbons increase with their molecular weight, although this is compensated to some extent by a decrease in volatility. The effects of the *chloro*-compounds may be related to the activity of the halogen contained in them. Chlorine is certainly more active in the aliphatic than in the aromatic compounds. For instance, the *chloro*-derivatives of naphthalene hold an intermediate position between the aliphatic *chloro*-compounds and chlorobenzene, both as to stability and toxicity.

The first cases of *poisoning by methyl chloride* in industry were reported by Gerbis in 1914

These were two men working in a chemical plant, who suffered from nausea, vomiting, and restlessness followed by somnolence, and then by dimness of vision which did not clear up for fourteen days after leaving work. Subsequently, forty-one cases were reported in Switzerland, Germany, and the United States, all of them employed upon making, installing or repairing refrigerators. The famous Chicago cases described by Kegel, McNally and Pope (1929) were most of them non-industrial. They recorded twenty-nine cases with ten deaths. Three of the non-fatal cases were industrial. There was a rise of temperature, pulse and respiratory rate, usually with oliguria and occasionally with suppression lasting up to forty-eight hours. Evidence of acute nephritis was found in about half the cases. Anæmia occurred in some of the men affected, the red cells dropping to as low as 3,100,000 per c mm and the hæmoglobin to as low as 50 per cent. Sometimes there was leucocytosis with a normal differential count.

The toxic effects of *methyl bromide* have been known since 1901, when Jaquet reported one case with vertigo, weakness, and temporary visual disturbances following a brief exposure, and two cases with the same symptoms, as well as asthenia and psychological disturbances, following more prolonged exposure. Since that date some forty-two cases have been reported, of which twelve were fatal and twenty-three recovered. In 1945, Clarke, Roworth, and Holling gave an account of poisoning occurring in four naval officers, two of whom died. They reported that a concentration of 1 per cent produces a marked irritation of the upper respiratory tract, headache, smarting of the eyes, abdominal discomfort, and numbness of the feet, which may last as a residual symptom for as long as four months. Death, when it occurs, usually results from pulmonary œdema. Lower concentrations, whilst producing these symptoms in milder degree, also cause delayed symptoms, visual disturbances, amblyopia, drowsiness and fits. Convalescence is characterized by depression and sleeplessness.

Besides these general symptoms, local contact with liquid methyl bromide produces severe characteristic vesicular burns. These are important in industry, and many workers making the substance have these blisters on their hands. Also, while fire-fighting with a methyl bromide fire-extinguisher, some of the liquid may get on the man's clothing, which it will readily penetrate. In 1945, Butler, Perry, and Williams described the cases of two soldiers who received burns in this manner after the liquid had penetrated army boots and anklets.

Garland and Camps (1945) have given an account of poisoning by methyl iodide, the symptoms are similar to those occurring with methyl bromide and methyl chloride.

Poisoning by *chlorinated naphthalene* may take the form of acne, particularly of the face, or of toxic jaundice produced by necrosis of the liver. The typical skin condition starts on the face, around the angles of the jaws or over the malar prominences, and from there spreads on to the sides of the face and on to the sides and back of the neck. The skin lesions in a typical case are comedones, papules, pustules and, in severe cases, small cysts. Sometimes the eruption spreads on to the shoulders and forearms (Jones, 1941).

In 1936, three fatal cases of jaundice in chlorinated naphthalene workers were recognized in the United States of America (Flinn and Jarvik, 1936-37, Drinker, Warren, and Bennett, 1937).

All three of the men were young and in none could any predisposing cause other than the industrial exposure be found to account for the illness. Two of the men who had worked side by side died within two months of each other. Both had been exposed to mixtures of *meta*- and hexachloronaphthalene, and one had been exposed to a mixture of tetra- and *meta*-chloronaphthalene with 10 per cent chlorinated diphenyl. In both, the diagnosis of acute yellow atrophy of the liver was made at necropsy. In the third case no necropsy was reported, but death occurred after an acute illness characterized by jaundice. In one case one had preceded the jaundice.

In addition to these fatal cases, Drinker, Warren and Bennett also mentioned four cases of non-fatal jaundice among subjects with similar exposure. No details were given. Greenberg, Mayers, and Smith (1939) recorded three fatal cases in young people working with chlorinated naphthalene and diphenyl. Two of the patients apparently had suffered from at least one previous attack of hepatitis, followed by a certain degree of improvement, before the fatal attack.

By attention to ventilation and medical supervision of workers the chlorinated naphthalenes and diphenyls can be handled in industry with safety. Education of the workers as to the cause of the acne must be undertaken and the necessity for personal cleanliness emphasized. Light coloured, highly starched, closely woven overalls with full length sleeves should be provided. These must be changed and laundered at least once a week. Adequate washing accommodation and locker space must be provided. The workpeople must be taught not to touch the skin with the hands and not to use rags for wiping the nose and the face. They must wash before meals and take food only in special rooms set aside for the purpose. Medical selection of workers must aim at avoiding adolescents and all persons with oily skins, established acne, or seborrhœa. Medical examinations must be carried out at least once a week. All early cases of acne or jaundice must be removed from contact with the toxic substance. Prevention of systemic effects turns upon exhaust ventilation to remove fume and dust, and avoidance of overheating of the wax.

INDUSTRIAL LUNG DISEASES

Substances handled in industry may attack the respiratory tract producing pneumoconiosis, inflammatory and allergic conditions, and also carcinoma. Inflammatory conditions have arisen in workers handling cadmium, beryllium, and vanadium. Cadmium metal is rarely used, but it is an important constituent of certain alloys. Its use is increasing for electro-plating iron and steel articles which were formerly zinc coated for purposes of rust proofing.

The first symptoms of industrial *cadmium poisoning* are dryness of the throat, cough, headache and vomiting. Later, symptoms arise in the respiratory system, and consist of pain and a sense of constriction in the chest, cough, dyspnoea, restlessness and prostration. If the dose is big enough, fatal broncho-pneumonia may occur. Unfortunately, the fumes of cadmium oxide have no pronounced odour or immediate irritant effect, and they can reach a fatal concentration without enough discomfort to drive the worker away from the source of exposure (Fairhall, 1945).

Bronchiolitis—Experimental work on the possible injurious effect of inhalation of the dust of molybdenum compounds or molybdic oxide fumes has shown that

shadows of silicosis. X-ray reticulation is caused in this instance by a mixture of coal dust and silica, and the disease is really an anthraco-silicosis. As a result of this work, the Workmen's Compensation Act was modified as it applies to miners, and such a man now gets compensation for pneumoconiosis and silicosis.

Aluminium and silicosis—There is conflicting evidence as to the effect of aluminium dust on the lung. It is important because it has been used extensively in the 1939-45 war for making incendiary mixtures and paints, and because there is evidence from Canada that the inhalation of aluminium dust will prevent silicosis in miners. The method has since been patented and this extraordinary move cannot but raise suspicions. Denny, Robson and Irwin (1939) exposed rabbits to metallic aluminium dust of particle size below 5μ and showed that fibrosis was produced, but Belt and King (1943) repeated these experiments on rats and showed that the rat's lung treated the particles as foreign bodies and formed small concretions surrounded by fibrous tissue. Repeated papers by Goralewski (1939, 1940, 1941, and 1943) from Germany ascribe various types of lung disease to aluminium dust. Crombie, Blaisdell, and MacPherson (1944) investigated 125 workers employed in the Pittsburgh stamp mills of the Aluminum Company of America, taking skiagrams of the chest of each man each year for three years. No abnormalities were found which could be attributed to the inhalation of the dust. Hunter, Milton, Perry and Thompson (1944) examined workers engaged in the grinding of duralumin propellers, and they were unable to find any changes in the lungs, although many of the men had been exposed for more than seven years to the dust, which was a mixture of aluminium and alumina.

In the last five years McLaughlin has done a great deal of work on the effect of iron oxide on the lungs. He showed in 1936 that electric arc welders tend to develop radiological changes of reticulation and even nodulation, and with Hardin (1945) he showed that similar changes could be produced by injecting iron oxide in the form of rouge into the trachea of rats. Necropsies on these animals and on one human being (Enzer and Sander, 1938) showed that iron oxide does not produce fibrosis of the lung, but if a lung is packed with this dust it surely must lose some of its elasticity, the lung being essentially an elastic organ. The changes occur not only in electric arc welders, but also to a lesser degree in oxyacetylene welders. McLaughlin, Grout, Barrie and Harding (1945) have also shown that silver polishers using jewellers' rouge develop reticulation as seen by X-ray. This may be due either to the iron oxide which is deposited in the lung tissue or to the silver, which they have shown to be deposited in the elastic layer of the arteries.

Boiler scalers' disease—Many authors have recently reported changes in the X-ray appearance of boiler scalers' lungs. Both flue dust and boiler scale contain substantial amounts of silica and iron oxide. Harding, Tod and McLaughlin (1944) have shown conclusively that the radiological changes are in part due to iron oxide and in part to silica. For six years they followed a boiler scaler whose lungs showed nodulation. He finally died with a carcinoma of the right upper lobe bronchus and they showed histologically that in fact he had silicosis.

Treatment of these dust conditions is essentially preventive. So far as steel

foundries are concerned, a full account of the necessary preventive measures was given in the report of a Committee set up by the Factory Department of the Ministry of Labour (1944). In order to reduce dust, the Committee recommended that effective measures be taken to prevent the escape of dust from blasting apparatus, and that efficient ventilating plant should be provided and kept in good repair and in continuous use. Workers can be prevented from inhaling dust by the use of suitable protective helmets which should be supplied with warm pure filtered air at a rate of not less than 6 cubic feet per minute. Helmets, gauntlets, overalls and other protective devices should be kept clean by vacuum cleaners, and there should be suitable storage accommodation provided close to every "blasting" enclosure. Suitable respirators should be provided for, and worn by, fettlers and dressers of steel castings. The Committee also advised that no person under eighteen years of age should be employed on or within 20 feet of any blasting apparatus, and that specially fine free silica used in moulding compositions, parting powders, and silica paint should be replaced by suitable non-siliceous substances, such as coloured aluminous fire clay (chamotte). A recent invention known as the hydro-blast has been installed in three foundries in England. A high velocity jet of sand and water is projected on to castings, thereby removing moulding material, cores and scale. The velocity of the water as it leaves the hydro-blast gun is in excess of 3 miles per minute. It can be readily understood that this apparatus has greatly improved the cleaning of castings, and much reduced the dust in the atmosphere of the fettling shops where it has been installed.

References

- Akatsuka, K., and Fairhall, L. T. (1934) *J Industr Hyg Toxicol*, **16**, 1
 Atkinson, A. D. S. (1944) "Fluorescent Lighting," London
 Bedford, T. (1944) *Brit J industr Med*, **1**, 31
 Belt, T. F., and King, E. J. (1943) *J Path Bact*, **55**, 69
 Bensath, A., and Varga, S. (1940) *Deutsch med Wschr*, **66**, 1194
 Berkovitch, M., and Israel, B. (1940) *Khmikaia Meditsina*, **18**, 117
 Browning, E. (1937) "Toxicity of Industrial Organic Solvents," *Industr Hlth Res Bd*, M.R.C. Rep., No. 80
 Butler, E. C. B., Perry, K. M. A., and Williams, J. R. F. (1945) *Brit J industr Med*, **1**, 30
 Clarke, C. A., Roworth, C. G., and Holling, H. E. (1945) *Ibid*, **1**, 17
 Colebrook, L., Gibson, T., and Todd, J. P. (1944) *Ibid*, **1**, 99
 Crombie, D. W., Blaisdell, J. L., and MacPherson, G. (1944) *Canad med Ass J*, **50**, 318
 Denny, J. J., Robson, W. D., and Irwin, D. A. (1939) *Ibid*, **40**, 213
 ——— (1939) *Industr Med*, **8**, 133
 Doig, A. T., and McLaughlin, A. I. G. (1936) *Lancet*, **1**, 771
 Drinker, C. K., Warren, M. F., and Bennett, G. A. (1937) *J industr Hyg Toxicol*, **19**, 283
 Dudley, H. C. (1938) *U.S. Pub Hlth Rep*, **53**, 281
 ——— (1941) *J industr Hyg Toxicol*, **23**, 470
 Enzer, N., and Sander, O. A. (1938) *Ibid*, **20**, 333
 Fairhall, L. T. (1936) *Ibid*, **18**, 668
 ——— (1945) *Phys Rev*, **25**, 198
 ———, Sayers, R. R., and Miller, J. W. (1940) *U.S. Publ Hlth Bull*, **253**, 5
 Farmer, E., and Chambers, E. G. (1926, 1929, 1939) *Industr Hlth Res Bd Rep*, No. 38, 55, 84
 ———, and Kirk, F. J. (1933) *Ibid*, No. 68
 Fawcett, R. (1943) *Brit J Radiol*, **16**, 323
 Flinn, F. B., and Jarvik, N. E. (1936-7) *Proc Soc exp Biol N.Y.*, **35**, 118

re-training, and the institution of appropriate means for his resettlement in suitable employment—is a joint concern of all, and a matter of vital importance to the national economy. No national health service will be adequate unless it includes full provision for such rehabilitation for one and all who would benefit from it. Service patients and civilians alike.

THE RANGE OF REHABILITATION

It is becoming generally recognized that prolonged immobilization, resulting from long illness or severe injury, produces a condition of physical deterioration which can only be effectively countered by active physical means. Muscles become atrophied, dependent soft parts oedematous, traumatized soft tissue is apt to become adhesive, joints stiff and bones decalcified. It is only by means of active exercises that circulation is properly maintained and the ill-effects of immobilization prevented or cured. This principle was first recognized in the *treatment of fractures* and the brilliant work accomplished by Robert Jones and his team laid the foundation for all future development in the sphere of physical rehabilitation. It was largely as a result of his successful work that there followed in due course the setting up of the B M A Committee on Fractures, the opening of fracture clinics with their attendant departments for rehabilitation and follow-up, and the Delevingne Inter-Departmental Commission on the rehabilitation of persons injured by accidents. It was thus only natural that when the present war broke out the medical departments of the armed Services and the Emergency Hospital Service of the Ministry of Health proceeded to organize, equip and staff special rehabilitation departments at all hospitals to which serious fractures or orthopaedic disabilities were to be transferred.

Burns and soft tissue wounds—It was soon found, however, that the same principles which were proving successful in the recovery of physical function after severe fractures were equally applicable to other forms of medical and surgical disability. Laceration of soft parts, extensive burns, or contaminated wounds involving the loss of tissue and the infection of deeper structures, all responded admirably to early movement, accompanied by appropriate physiotherapy and light occupational therapy. Griffiths has long advocated the use of small impervious dressings of cellophane or vizad, followed by regular finger exercises, in the case of injuries or infections of the hand, and Grossmark and Plewes (1945) have shown that even in the case of suppurative tenosynovitis, aspiration of the pus followed by the instillation of penicillin into the tendon sheath will result in most cases of quick recovery without adhesion or open operation, if accompanied by regular methods of rehabilitation.

Breathing and abdominal exercises—The application of physical methods to the restoration of vital capacity after serious affections of the chest has been carefully studied at Brompton Hospital and other chest centres, and a successful technique evolved. Patients who are to undergo serious thoracic operations—lobectomy, pneumonectomy, thoracoplasty—go through a special course of breathing exercises before operation, which are repeated throughout the whole post-operative stage, and similar methods are employed in the treatment of cases of pneumonia, empyema, emphysema and other pulmonary conditions associated with respiratory defects or lack of chest expansion. Special courses of exercises have been adapted for use in the treatment of bronchial asthma and of bronchiectasis. The applic-

bility of methods of rehabilitation to cardiac disorders has been the subject of a special memorandum, issued by the Cardiac Society in 1944, in which attention was drawn to the type of patient likely to benefit by active methods of exercise combined with appropriate occupation

Experience at Service and E M S hospitals during the present war has clearly proved that the incidence of post-operative chest complications and of recurrent hernia has been largely reduced by the adoption of a carefully planned course of breathing and abdominal exercises, both before and after operation, and Shorter (1944) has described the methods of rehabilitation which have been carried out with success in various forms of abdominal surgery. It is claimed that the risk of thrombosis and of visceral prolapse is considerably reduced by the adoption of such measures, and a similar claim is made for the routine use of abdominal exercises after child-birth. There is reason to suppose that gastric and intestinal disorders, involving long periods of rest in bed, would also react favourably to a well-planned programme of rehabilitation exercises and occupational therapy, and there is room for considerable research and experiment in this field.

The modern treatment of neurosis, in all its forms, is largely dependent upon the combination of skilled psychotherapy and expert rehabilitation technique. Functional disorders, hysteria in its varied forms, anxiety neurosis, effort syndrome, post-concussional vertigo and other types of disturbed mental equilibrium are treated to-day, not only by psychiatric investigation, narcosis, insulin and electric shock therapy, but by a carefully balanced programme of physical exercise, team games and selective occupational therapy. So successful has this proved that the Mill Hill Neurosis Centre has been able to report that of 559 consecutive cases of neurosis sent back to the Army during 1941, over 70 per cent were serving efficiently six months later, whilst of 200 cases of effort syndrome returned to duty during the same period, 82 per cent were settling down happily and usefully in Army life. At Roffey Park, where cases of nervous breakdown in industry form the chief subjects for rehabilitation, the first year's report shows 82 per cent. happily resettled in employment, out of 200 cases followed up.

The heavy incidence of *peripheral nerve injuries* during the present war has opened a wide field for rehabilitation methods. During the long period that must necessarily elapse between suturing operations and the recovery of motor and sensory function, weak or paralysed muscles must be maintained in tone and gradually strengthened, poor circulation improved, contractures prevented and coordination developed. Hydrotherapy, massage, electrical stimulation, careful splintage, finger exercises and special forms of occupational therapy all play their part in restoring physical function, provided the affected nerve is not irretrievably destroyed, and at the same time help to sustain the patient's morale and secure his active cooperation in his ultimate recovery.

Plastic surgery presents a somewhat similar problem, especially in patients who have sustained extensive loss of tissue, necessitating numerous operations. Here, again, the combination of physiotherapy, games and suitable handicrafts not only contributes towards the production of healthy, supple grafts, mobile joints and dexterous movement of injured fingers, but helps to dissipate the apprehension and depression from which such patients are only too apt to suffer. McIndoe (1943) has well pointed out that the "rehabilitation of patients requiring plastic repair

is an essential part of treatment," and must take the form of "a carefully planned prescription, embodying both psychological and physical remedial ingredients."

The field of rehabilitation is by no means exhausted with the examples given. The re-education of patients who have lost one or both limbs, the special treatment of the blind and of deaf-mutes in preparation for useful and satisfactory employment, the combination of graded exercise and sheltered employment in the tuberculosis sanatorium or colony, the use of manipulative surgery and remedial exercises and handicrafts in the treatment of chronic arthritis, the special clinics and hospitals for the treatment of children with congenital deformities and other forms of orthopaedic disability—all represent conditions to which appropriate forms of medical rehabilitation are applicable, and without which treatment can never be complete.

THE TECHNIQUE OF REHABILITATION

The basic principles which govern the technique employed in the restoration of physical and psychological function after serious illness or injury, are fundamentally the same whatever the nature of the disability. They involve the combined use of physiotherapy, physical exercise alternating with periods of complete relaxation, occupational therapy and heavy handicrafts, remedial games, music, recreation and stimulus, psychological adjustment, and vocational guidance. The carrying out of such a programme requires the services of a team of trained workers, each with his or her allotted task, but all combining in a common effort. Meeting from time to time in conference to discuss their common problems and difficulties. At the head of the team is the physician or surgeon in charge of the case, who prescribes the particular forms of rehabilitation activity suitable for each patient (usually on a separate rehabilitation prescription form), changing the prescription from week to week as the patient becomes fit for more strenuous activities. The same physician or surgeon maintains medical supervision of the case throughout the whole period of rehabilitation, wherever such supervision is possible, but the actual task of superintending the rehabilitation exercises, training the team and watching the patient's reactions from day to day, is relegated to a special rehabilitation medical officer, where available. He may be an expert in physical medicine, or a member of the junior medical or surgical staff of the hospital, but it is essential that he should be thoroughly familiar with all the details of modern rehabilitation methods, and able to devote sufficient time to this important work. The various activities included in the programme are carried out by trained physiotherapists, physical training instructors or instructresses, occupational therapists and workshop instructors, whilst the Army Educational Officers and Welfare Officers, the hospital almoners and social workers, and the disability rehabilitation officer of the neighbouring employment exchange, look after the mental, psychological and vocational aspects of the subject.

The initial stages of rehabilitation necessarily take place in the hospital ward and out-patient department, for it cannot be sufficiently emphasized that rehabilitation is an integral part of medical and surgical treatment, and should begin as early as possible after the onset of illness or accident. In the later stages, however, as Watson-Jones (1942) has persistently urged, it is a great advantage if the patient can be removed from the hospital atmosphere to a residential rehabilitation centre in country surroundings, where there are ample facilities in the shape of ground

ing fields, swimming pools and opportunities for different forms of light and airy handicraft

The general regime—Each patient is provided with a programme of his day's activities, increasing in amount and time as he progresses in physical strength, and consisting of periods for physiotherapy (mostly active remedial exercises other than passive measures), group exercises in wards or gymnasium, occupational handicrafts (both diversionary and remedial) and games, whilst other parts of the day are devoted to rest periods, medical or surgical treatment and opportunities for mental exercise or entertainment. A well-stocked hospital library, such as that organized so successfully at the Southern Hospital, Dartford, is a valuable adjunct to this aspect of rehabilitation, whilst for long-stay patients opportunities are now available for the pursuit of educational courses, with textbooks and instructional aid provided by the educational authorities. Exercises and remedial games are conducted out of doors whenever possible, patients being grouped for the purpose according to their type of disability and stage of recovery. The association with other patients, and the competition of exciting team games, prove a valuable stimulus to the more timid and cautious type of patient.

The later stage—Interesting experiments have recently been carried out in the use of industrial machines in the terminal stages of medical rehabilitation, thus replacing the somewhat artificial atmosphere of the occupational therapy department with something more purposeful and allied to normal employment. The first experiment was made by Gissane and the Austin Motor Company, as a result of which the Company has fitted up a Rehabilitation Workshop at their own factory, equipped with machines operated by a variety of different movements, each providing facilities for the exercise of particular muscle-groups, as ordered by the surgeon. Employees of these particular works are thus enabled to take part in gainful employment whilst actually completing the rehabilitation of a particular part of the body which has been injured, the whole process being supervised by the industrial medical officer. A variant of this experiment has been put into practice at the Queen Victoria Plastic Unit, East Grinstead, where patients suffering from damaged hands and requiring delicate exercise of the finger muscles, take part in fine assembly work at a small factory which has been set up adjoining the hospital, whilst at Hill End Hospital, St. Albans, arrangements have been made with a large industrial works for patients to be employed for a limited period each day on different forms of light machine work suited to their particular disabilities, and affording steady exercise for the particular muscles which need further rehabilitation.

THE GOAL OF REHABILITATION

The main purpose of rehabilitation is not attained at the hospital door, even in the case of patients who hope to return to their former employment. It is not attained at the factory door, when the patient reports back for duty. It is not reached until sufficient time has elapsed to show that the disabled man has so far recovered his physical capacity, or has been so successfully re-trained for a more suitable vocation that he can hold down his new job without undue strain or risk of relapse. In other words, the prime purpose of rehabilitation is to see a man through, from hospital ward to suitable occupation in life, and this necessitates the closest possible liaison between hospital staffs, employment exchanges and industry.

The task of resettlement is mainly an industrial matter, and the Ministry of Labour has already taken important steps to implement the findings of the Disabled Persons (Employment) Act. Disablement rehabilitation officers have been appointed to all the chief exchanges, and are undergoing special training; arrangements have been made for them to visit hospitals and interview all patients likely to require vocational training; an industrial rehabilitation centre has been opened at Egham, where men who need to change their occupation can be physically reconditioned and can receive expert industrial guidance and advice, the Government training centres receive and train, at Government expense, all disabled people likely to profit by such a course, and plans are already on foot for the provision of sheltered industries for those unable to compete on equal terms with those who are not physically handicapped. But excellent as all these plans are, they will fail in their ultimate purpose unless there is clear medical direction and supervision throughout. Rehabilitation is essentially part of medical treatment, and the man who is partly disabled from illness or injury, and has received medical rehabilitation at hospital, can never be satisfactorily resettled in employment unless the medical knowledge of his physician or surgeon, as to his ability and disability, is linked up to the industrial knowledge of the disablement rehabilitation officer, the works medical officer or the shop manager, as to the work that is available and the mechanical and psychological stress involved in each particular process. This means that there must be clear guidance from the hospital, on the special form which has been prepared for the purpose, showing, in simple terms, just what the disabled person can and cannot do, careful job-analyses of the processes in industry, prepared by works medical officers or other industrial representatives, free consultation between hospital staffs, almoners and employment officials regarding all difficult cases, and a strict system of review and follow-up at regular intervals.

Various experiments are being made at certain hospitals with a view to bridging the difficult gap between the discharge of patients from hospital and their employment in suitable occupation. These experiments include the holding of regular conferences between surgeons or rehabilitation medical officers, almoners and employment exchange officials, the organization of special rehabilitation committees, consisting of representatives of hospital lay and medical staffs, local industry, trades unions, welfare organizations and labour offices, the appointment of lay rehabilitation or "field" officers at two hospitals, to advise and help patients during their period of hospital rehabilitation and also in securing suitable employment on leaving, and the periodic review of all patients discharged with a disability.

"The debilitated person," as Ancel Keys (1945) has pointed out, "is not restored to full health when he no longer needs the rather ritualistic routine of hospital bedcare. Deconditioning is a necessary part of many diseases, but reconditioning is not necessarily automatic when the disease has run its course."

References

- Cardiac Society (1944) *Brit med J*, **1**, 565
 Grossmark, G. J., and Plewes, L. W. (1945) *Ibid*, **1**, 906
 Keys, A. (1945) *Surg Clin N Amer*, **25**, 442
 McIndoe, A. H. (1943) *Postgrad med J*, **19**, 161
 Shorter, A. (1944) *Lancet*, **1**, 243
 Watson-Jones, R. (1942) *Brit med J*, **1**, 403

ARTHRITIS AND CHRONIC RHEUMATISM

By DOUGLAS H. COLLINS, M.D.

Emergency Medical Service Medical Superintendent and Pathologist, Wharfedale Hospital, Sheffield, Rheumatism Research Fellow, University of Leeds

THE great advances in medical knowledge during the war have an indirect rather than a direct application to the problems of rheumatism. No great mysteries have been solved nor the panacea discovered. But lessons have been learnt which, if rightly applied, will certainly advance the care and treatment of patients with arthritis and rheumatism. In order of importance may be named —

- (1) The ready availability of specialist services such as exist in the medical organization of the Forces and in the Emergency Medical Service
- (2) The revolutionary escape from empiricism in treatment consequent upon the growth of chemotherapy
- (3) New developments in the institutional care, rehabilitation and social after-care of the chronically disabled
- (4) An enhanced knowledge of the functions, and derangements of joints, muscles and nerves

Of these only the first will be enlarged upon. Many a rheumatic sufferer in the Services, unemployable on account of his symptoms, embarks on an Odyssey of reference from one specialist to another. This is not just a case of "buck passing" — it is a prerequisite to successful treatment and should form the basis of any future rheumatism organization. Often it is only thus that the patient can be correctly placed for treatment. Time can, of course, be saved when the patient is first seen by a physician experienced in rheumatic diseases, who can either determine treatment or direct him to the appropriate specialist department. This is being done in certain establishments of the British and American Forces.

Rheumatism is not to-day a sufficient diagnosis. No patient is discharged from the hospital I now serve with the plain label of rheumatism, although many are so admitted. Large specialist units of orthopaedics, neurology and psychiatry are here gathered together, and the rheumatic label becomes converted into one appropriate to the department where final treatment and advice can best be secured. Only acute rheumatism (rheumatic fever) remains entirely within the province of the general physician.

In what follows, frequent reference will be made to advances in etiology, because intelligent treatment to-day demands the deepest knowledge of the causation of symptoms.

Comroe (1945) writes —

"Some practitioners unfortunately treat arthritis patients for long periods without first establishing a definite diagnosis. Every effort should be made to diagnose the type of arthritis as soon as possible. This does not mean, however, that affected joints should not be splinted or that mild analgesics should not be given during periods of study of the patient."

In passing, this paper of Comroe's on common mistakes in handling arthritic patients will well repay studious reading.

SPECIFIC INFECTIVE ARTHRITIS

Since most bacterial infections of joints respond well to modern chemotherapy every early case of joint disease which has the appearance of being of an inflammatory nature should be carefully reviewed with this diagnosis in mind. Fever, systemic toxicity, raised sedimentation rate and leucocytosis are important indices. Diagnosis is established by recovery of significant micro-organisms on culture from the joint and sometimes from the blood, by the aspiration of a highly cellular joint exudate and, in some instances, by estimation of serum antibodies.

Suppurative arthritis due to pyogenic infection of the joint is usually non-articular. Its treatment by local or systemic penicillin has revolutionized the prognosis, but it remains a matter largely for the surgeon and will not be discussed further.

Gonococcal arthritis may follow up to a month or more after venereal infection. In its subacute form it may readily be mistaken for rheumatoid arthritis or rheumatic fever. It is often polyarticular, tending to affect the knees and ankles, but also other joints. A history of genital infection, moderate blood leucocytosis and a high polymorphonuclear count in the joint exudate warrant an attempt at specific therapy, as the missed case may be disastrous in its results. Gonococci are not always recovered from the joints, but the blood gonococcal complement fixation test usually becomes positive in course of time. The joints must be completely rested to limit the destruction of articular tissue. A full oral course of sulphonamides must be undertaken. Sulphamezathine or sulphadiazine, 2 gm. six-hourly, should be given for six days, followed by the usual tailing off of the dose for a further thirty-six hours. It is valuable to check the treatment by occasional estimation of sulphonamide in the blood and by leucocyte counts. This treatment almost always cures the early gonococcal arthritis, but penicillin may be required in the case of infection by sulphonamide-resistant strains of the organism, and should be used if sulphonamides fail in the proven gonococcal infection. It must be remembered, however, that rheumatoid arthritis is a far more likely diagnosis if sulphonamides fail to relieve a suspected case in which gonococcal infection remains unproved.

Meningococcal arthritis occurs in the course of cerebrospinal fever and infrequently also as a manifestation of chronic meningococcal septicæmia (Copeman and Stewart, 1942). The latter is diagnosed by blood culture. It yields to sulphonamides given as above.

Undulant fever is frequently accompanied by arthritis of the large joints. The diagnosis is obtained by the finding in the blood of significant agglutinin titres for *Brucella*, or by special blood culture methods. This disease should be remembered when arthritis is associated with a relapsing pyrexia. Treatment is not always satisfactory, but sulphonamides ought to be tried.

Dysenteric arthritis is associated with bacillary dysentery. It is generally uncommon in this country, where the milder forms of Flexner or Sonne type infections prevail.

Tuberculous arthritis is customarily monarticular. An insidious monarticular onset, however, is seen in some cases of multiple non-specific arthritis (Collins and

Lameron, 1936) Expectant treatment, which includes full rest of the joint, should be adopted in all cases of slowly progressive inflammatory infection of a single joint, and the patient should be referred to an orthopaedic surgeon should the condition then not resolve

RHEUMATOID ARTHRITIS

The clinical characters of this disease are well known. In its onset, course, pathology and systemic manifestations there are strong reasons to regard it as an inflammatory disease caused by an unidentified infective agent. Non-specific infective polyarthritis is a good synonym, which brings to mind the rationale of the best modern lines of treatment

Pathology—The gross and microscopic appearances of affected joints and their exudates are those of inflammation and suggest chronic infection. Gross suppuration does not occur. Bacteria are not recovered and the search for virus elementary bodies, which raised hopes a few years ago, has now been abandoned. Experimental arthritis has been produced by all manner of means in various rodents. Recently Selye *et al* (1944) induced arthritis in rats by large doses of adrenal cortex hormone, but this also required the removal of one kidney, the feeding of salt and, in some instances, thyroidectomy. These multiple assaults render the application of the experimental results somewhat questionable. In any case, rodent joints differ in important respects from joints of larger animals and are notoriously easy to insult. Both naturally occurring and experimentally induced chronic proliferative arthritis of swine, as a consequence of systemic infection by *erysipelothrix rhusopathiae*, were described by Collins and Goldie (1940). The experiments seemed to show the possibility of inflammatory tissue changes persisting in certain joints after the disappearance of the infecting micro-organisms originally lodged in the joints during a transient bacteraemia. Bacteria reaching the joints in minimal numbers can start tissue reactions which continue after the infecting organisms have been destroyed. This behaviour of joint tissues may reconcile the chronicity of arthritis of rheumatoid type with the sterility of the joints. Although *erysipelothrix* sometimes infects man, no evidence has been found from extensive serological studies that this particular type of organism might be a cause of human chronic arthritis.

Unfortunately the etiological agent of rheumatoid arthritis is unknown and chemotherapeutic measures cannot be specifically applied. None the less, I am convinced that other lines of treatment of rheumatoid arthritis should be approached from the same direction as the treatment of other types of infective arthritis.

Relation with rheumatic fever—Baggott and Rosenberg (1941), and Young and Schwedel (1944) have found cardiac lesions of the rheumatic type in something like 60 per cent of cases of rheumatoid arthritis brought to autopsy. In most instances the cardiac disease was unsuspected during life. The former authors found, in comparison, only some 5 per cent. rheumatic heart lesions in unselected autopsy material. These facts, coupled with the transition of clinically typical rheumatic fever into chronic rheumatoid arthritis, which is occasionally observed, lend support to the view that the latter disease may be a "lente" form of the other

The association of hæmolytic streptococcal infection is less obvious with rheumatoid arthritis than with rheumatic fever. Salicylate therapy does not have the beneficial effect in the chronic disease that it has in the acute.

TREATMENT—So far, no way of preventing rheumatoid arthritis is known. Seen in the early stage with one or two acutely painful, swollen joints, bed rest must be prescribed. Specific infective arthritis should be carefully excluded. If in doubt and the disease is early with slight pyrexia, it is worth while instituting a course of sulphonamides, but the prognosis should be guarded, as these drugs are not likely to have any appreciable effect on non-specific rheumatoid arthritis. Salicylate compounds can be given freely for the pain and comforting application prescribed for the joints. Penicillin, unhappily, even in high dosage, has no effect on the course of the disease (Boland, Headley and Hench, 1944).

When faced with a painful, swollen, hot joint, either at the outset or at an flare-up incident in the course of the disease, picture the underlying pathology. Within the joint there is an œdematous, vascular, proliferating synovial membrane congested and red, infiltrated with inflammatory cells, creeping over and eroding the articular surfaces and pouring out a cellular exudate. As in the case of any other inflammation, this joint needs rest. Complete rest is obtained excellently by plaster splinting. Weight bearing and any degree of movement sufficient to cause pain must be prohibited. Intractable ankylosis results, not from immobilization, but from progressive destruction of the articular surfaces, which is favoured by continued motion.

"Complete and prolonged rest is the keynote to successful treatment of this disease" (Cecil, 1944). Rest in bed during the acute or early stages of the arthritis and local rest to selected joints by properly fitting splints, will eliminate much of the chronic disability that so surely follows less rigid attempts at treatment. Pain will be relieved by proper splinting. The joint need not be moved at all for seven to ten days. Thereafter it is well to take the limb from the splint and passively exercise it daily through its range of painless movement, which will increase on each occasion. Weight bearing should be avoided until all signs of active inflammation in the joint are past.

Analgesics, such as aspirin or A.P.C. tablets, should be given freely, especially at night in order to obtain restful sleep. Amidopyrine must not be used for any long period of time.

Diet—Restrictions and dietary fads are unwarranted. Diet should be full, with tonic, appetizing mixtures, if indicated, and a normal vitamin intake.

Gold is a valuable therapy in all active and progressive cases. Myocrisin or solganol are largely used and appropriate courses are scheduled by the manufacturers. Repeated small courses totalling 0.5 gm. are, in general, much safer and as effective as fewer but larger courses. Gold treatment is most successfully combined with a plan of local and general rest as outlined above.

Physiotherapy—Contraptions for applying local heat can often be made by a resourceful patient and an ingenious practitioner, using, with due safety precautions, the domestic electric fire or reading lamp. Daily treatment at home by simple methods can be of more benefit than interrupted treatment at a clinic involving tiring journeys. Contrast baths with one-minute alternating immersions

of hands or feet into cold tap water and hot water of a hot-bath temperature are beneficial in relieving the more chronic stages of the disease in the small peripheral joints. Non-weight-bearing movements can be demonstrated to the patient and leg movements can be performed with advantage in the household bath. Skilled massage and electrotherapy are important after immobilization has relieved the acute phase. Hydrotherapy at the spas is of great value at this stage but, as Jarman (1943) writes, "a spa is not the best place to treat a patient whose disease is so active as to require a splint," unless suitable institutional care is also provided.

Focal infection—Never promise a patient that removal of septic foci will cure his disease. Elimination of definite foci of infection is advisable on the grounds that the patient's powers of resistance will then have less to battle with. A few cases of rheumatoid arthritis certainly improve after this measure, but the balance of evidence is against a close etiological relationship between focal infection and arthritis. A dental surgeon should advise on which teeth should be extracted and an ear, nose and throat surgeon should be consulted if chronic infection in sinuses or throat is suspected.

OSTEOARTHRITIS

Primary (idiopathic) osteoarthritis is essentially the result of wear and tear upon ageing joint tissues. Cartilage degenerations and the reactive hypertrophic changes of cartilage and bone resulting in typical osteoarthritis may also supervene as a secondary manifestation of other joint diseases and deformities (Collins, 1939). The absence of X-ray changes does not rule out a diagnosis of osteoarthritis. The stage of cartilage destruction without bony reaction can be severely painful and may last for a long time. On the other hand, the X-ray demonstration of gross hypertrophic bony lipping, particularly in the spine, is not necessarily related to symptoms. Consideration must be paid to clinical signs, restricted movement and friction.

The best *treatment* is based on orthopædic principles, and drugs, apart from analgesics, are of little use. Early lesions of cartilage may heal if the painful joint is rested without weight bearing. Rigid splinting is not indicated. Rest in bed with a little passive movement seems often to prevent the development of a chronically painful joint and deformity. The diet of obese patients should be adjusted with a view to weight reduction. Small daily doses of thyroid extract may be helpful in persons of the obese, hypothyroid type. All sufferers should be advised in detail how to avoid further trauma to the joints affected.

GOUT

The practitioner should be alert to the possibility of gout in cases of intermittent acute monarticular arthritis in males with complete remission between the attacks. Gout still occurs in all classes of patients and the early disease is frequently misdiagnosed. Cases with tophaceous deposits are more obvious. Colchicine, 1/60 grain by mouth for four or five doses, will relieve the acute attack. The treatment of the chronic forms is complex and cannot be elaborated here. Reference

should be made particularly to Hench's writings on the subject (Hench, 1941) or to standard works on treatment

SPONDYLITIS ANKYLOPOIETICA

This grave, progressive and disabling disease of the spine demands expert orthopaedic management. Radiographic changes in the spine are usually preceded by evidence of sacro-iliac arthritis, although Fletcher (1944) shows that a few other, atypical cases occur without that evidence. X-ray treatment is worth while in even an active case of the disease (Hilton, 1943). These patients ought to be hospitalized early. Only by skilful nursing and physiotherapy can the necessary treatment be maintained. I have been deeply impressed by the exceptionally good results achieved in servicemen developing this disease who have had the advantage of early, prolonged hospital treatment with efficient radiotherapy.

FIBROSITIS

This rather inappropriate term for most conditions of non-articular rheumatic disease is justified only by common usage. To help in planning treatment, four common etiological types of fibrositis may be borne in mind —

(1) *Toxic* myalgia associated with, or immediately following, various system intoxications or infections

(2) *Mechanical* related to acute or repeated strains of ligaments and muscle insertions

(3) *Postural* muscle spasm resulting from injury or disease of joints or from developmental or occupational deformities

(4) *Psychogenic* Halliday (1937) drew attention to the high proportion of compensation insurance cases in which rheumatic complaints were due to psychogenic factors. Boland and Corr (1943) found psychogenic rheumatism to be a frequent cause of disability among rheumatic patients admitted to a U.S. service hospital. They state that the diagnosis is facilitated by recognizing such points as gross incongruity of symptoms with structural changes, persistence of disability, bizarre posture and associated hysterical manifestations. Ellman and his colleagues (1944) examined psychologically fifty mixed service and civilian patients diagnosed as fibrositis of over three months' standing. They found thirty-five to be suffering from common psychological disorders bearing on their complaint. Hysterical features were most common. They state that vague shifting pains suggest an underlying emotional disorder, whilst strictly localized pain points to the presence of organic changes.

Copeman and Ackerman (1944) offer an anatomical explanation of that further form of fibrositis associated with tender, palpable nodules. These nodules are apparently vascular, fatty structures liable to oedema and congestion, in which state they may impede the smooth working of muscles and tendons in their fibrous envelopes or even herniate through foramina in the fascial investments.

TREATMENT —Therapeutic infiltration of a local anaesthetic is now an established procedure when pain is referred to accessible tender spots, but good results

not constantly achieved Steinbrocker (1944) has described the saline-procaine as a diagnostic aid —

The point of maximum tenderness is located and a skin wheal formed by intradermal injection of procaine. Then 2 or 3 c cm of normal saline are injected subcutaneously through the wheal. The spot is palpated again ten or fifteen minutes later. Immediate relief of pain and tenderness at this stage suggests a psychogenic basis for the complaint. If, however, symptoms continue, a needle is passed again through the wheal to a reasonable depth until the trigger point which induces the characteristic pain is touched, when 5 or 10 c cm per cent procaine are injected. A somatic basis of the pain is probable if relief is now and further treatment by infiltrations of procaine is encouraged.

The diagnostic value of this technique is not absolute because the symptoms of pure hysteric may withstand both parts of the test, or, on the other hand, psychosomatically determined symptoms may withstand the saline and yield at first to the procaine but relapse when the suggestive influence of the new line of treatment falls off.

Success in treating fibrositis requires a careful consideration of all possible factors. Vigorous massage and physiotherapy undoubtedly relieve many early and acute cases. In chronic cases, search must be made for underlying causes and treatment directed appropriately. At present, more importance attaches in America to psychogenic rheumatism than in this country. The war has vastly increased the appreciation of psychosomatic medicine. It has also brought psychiatric training and experience to a great number of practitioners. There is hope that a nationally available specialist psychiatric service will grow after the war. This will do much to relieve both practitioners and patients of their wearisome burden of fibrositis.

References

- Baggettoss, H., and Rosenberg, E. F. (1941) *Arch int Med*, 67, 241
 Boland, E. W., and Corr, W. C. (1943) *J Amer med Ass*, 123, 805
 —, Headley, N. E., and Hench, P. S. (1944) *Ibid*, 126, 820
 Cecil, R. L. (1944) "A Textbook of Medicine," 6th edition, Philadelphia and London, 1305
 Collins, D. H. (1939) *Brit J Rheum*, 1, 746
 —, and Cameron, C. (1936) *Brit J Surg*, 24, 23
 —, and Goldie, W. (1940) *J Path Bact*, 50, 325
 Comroe, B. L. (1945) *J Amer med Ass*, 127, 392
 Coperman, W. S. C., and Ackerman, W. L. (1944) *Quart J Med*, 13, 37
 —, and Stewart, W. (1942) *Lancet*, 1, 603
 Ellman, P., et al (1942) *Ann Rheum Dis*, 3, 56
 Fletcher, E. (1944) *Lancet*, 1, 755
 Halliday, J. L. (1937) *Brit med J*, 1, 213, 264
 Hench, P. S. (1941) *J Amer med Ass*, 116, 453
 Hilton, G. (1943) *Proc roy Soc Med*, 36, 608
 Jarman, M. B. (1943) *J Amer med Ass*, 123, 631
 Selye, H., et al (1944) *Ibid*, 124, 201
 Steinbrocker, O. (1944) *Ibid*, 125, 397
 Young, D., and Schwedel, J. B. (1944) *Amer Heart J*, 28, 1

should be made particularly to Hench's writings on the subject (Hench, 194) or to standard works on treatment.

SPONDYLITIS ANKYLOPOIETICA

This grave, progressive and disabling disease of the spine demands expert orthopaedic management. Radiographic changes in the spine are usually preceded by evidence of sacro-iliac arthritis, although Fletcher (1944) shows that a few atypical cases occur without that evidence. X-ray treatment is worth while in every active case of the disease (Hilton, 1943). These patients ought to be hospitalized early. Only by skilful nursing and physiotherapy can the necessary treatment be maintained. I have been deeply impressed by the exceptionally good results achieved in servicemen developing this disease who have had the advantage of early, prolonged hospital treatment with efficient radiotherapy.

FIBROSITIS

This rather inappropriate term for most conditions of non-articular rheumatic disease is justified only by common usage. To help in planning treatment, the common etiological types of fibrositis may be borne in mind—

(1) *Toxic* myalgia associated with, or immediately following, various system intoxications or infections

(2) *Mechanical* related to acute or repeated strains of ligaments and muscle insertions

(3) *Postural* muscle spasm resulting from injury or disease of joints or from developmental or occupational deformities

(4) *Psychogenic* Halliday (1937) drew attention to the high proportion of compensation insurance cases in which rheumatic complaints were due to psychogenic factors. Boland and Corr (1943) found psychogenic rheumatism to be a frequent cause of disability among rheumatic patients admitted to a U.S. service hospital. They state that the diagnosis is facilitated by recognizing such points as gross incongruity of symptoms with structural changes, persistence of disability, bizarre posture and associated hysterical manifestations. Ellman and his colleagues (1944) examined psychologically fifty mixed service and civilian patients diagnosed as fibrositis of over three months' standing. They found thirty-five to be suffering from common psychological disorders bearing on their complaint. Hysterical features were most common. They state that vague shifting pains suggest an underlying emotional disorder, whilst strictly localized pain points to the presence of organic changes.

Copeman and Ackerman (1944) offer an anatomical explanation of that form of fibrositis associated with tender, palpable nodules. These nodules are apparently vascular, fatty structures liable to oedema and congestion, in which state they may impede the smooth working of muscles and tendons in their fibrous envelopes or even herniate through foramina in the fascial investments.

TREATMENT—Therapeutic infiltration of a local anaesthetic is now an established procedure when pain is referred to accessible tender spots, but good results

few of the more interesting developments. Some examples illustrate highly chemical developments, others are of more general therapeutic application.

THE ELECTRO-DIAGNOSIS OF PERIPHERAL NERVE LESIONS

Important advances have been made by the introduction of electro-myography into clinical practice and by developments of the classical muscle-testing technique. In order to appreciate the new work it is necessary to recall the limitations of the established methods. In the past, motor nerves and muscles have been examined by means of faradic and galvanic currents applied to the overlying skin or by direct stimulation when the muscles and nerves were exposed at operation, the latter method is of limited application only. The response of muscle and nerve depends upon both the intensity and duration of the exciting current, a current of shorter duration needing to be of greater intensity to stimulate a given muscle or nerve, and conversely. Innervated muscles respond to electrical stimulation by a brisk twitch and denervated muscle fibres by a characteristic sluggish or vermiciform contraction.

In practice, the faradic current (duration about 0.001 second) causes a contraction in normal muscle by stimulating the motor nerve, but fails to stimulate denervated muscle, because the current intensity required is intolerably high at such short duration. The galvanic current (duration 0.2 to 0.02 second) excites a brisk twitch in normal muscle by stimulating the motor nerve and, by virtue of the relatively long duration, the characteristic sluggish response in denervated muscle. Thus it is possible to obtain qualitative estimations of the state of peripheral nerves and muscles, but quantitative estimations of recovery or degeneration at intervals in treatment are impracticable because the variable resistance of the skin modifies the intensity and duration of the applied currents.

Chronaximetry—Stimulation by means of condensers charged to a pre-determined intensity and having a known duration of discharge has been used in an attempt to measure the intensity/duration factor of muscles and nerves (*chronaximetry*), but the variable skin resistance again introduces an incalculable modification of the current.

By patient study of the physical and biological problems involved, Bauwens (1941, 1943) has utilized modern developments in the thermionic valve to develop an apparatus which eliminates the factor of skin resistance and makes possible transcutaneous stimulation by currents of pre-determined wave form, intensity and duration. Thus clinical *chronaximetry* now permits of quantitative and qualitative estimations of the electrical reactions of muscle and nerve. However, as Bauwens has pointed out, there is still the problem that when both normal and denervated fibres are present, the intensity/duration factor (*chronaxie*) is modified according to the relative proportion of normal and abnormal fibres, although not in such a way as to give an indication of the absolute proportion of each type of fibre. For this reason the method is only of limited value for estimating progress at consecutive examinations.

Electro-myography—The development of clinical electro-myography by Weddell (1943) and other workers has added a new and most valuable diagnostic method to the study of peripheral nerve lesions. The electrical reactions so far considered

represent the response of muscle and nerve to externally applied currents. Electro-myography is concerned with minute electrical potentials which occur in muscles and nerves under certain conditions. These are the physiological currents associated with nerve impulse and muscle contraction and are comparable to those occurring in the brain (electro-encephalography) and the heart (electrocardiography). The potentials concerned in electro-myography are of the order of micro-volts, and it is due to recent improvements in thermionic valve amplifying circuits that it has become possible to record and measure these minute currents without undue distortion.

The potentials are collected by means of a bipolar needle inserted into nerve or muscle bundles. When the patient attempts voluntary contraction, normal muscles and nerves develop showers of bi-phasic potentials (action potentials) but none occur at physiological rest. In denervated muscles, small mono-phasic potentials (fibrillation potentials) occur at fairly regular intervals, independently of rest or attempted voluntary contraction. Muscle fibres which have died and been replaced by fibrous tissue reveal neither action nor fibrillation potentials. Muscles which contain a mixture of normal and denervated fibres show both action and fibrillation potentials, thus estimation of the proportion of each type from time to time will indicate whether recovery or the reverse is taking place. Until recently, there has been no satisfactory method to measure the number and strength of the action or fibrillation potentials in a particular muscle. This year Bauwens, in a paper read to the British Orthopædic Association, has described a practical method for measuring action potentials. This latest development makes possible quantitative estimations of recovery or degeneration.

The electro-myograph is the most accurate method of electro-diagnosis in peripheral nerve lesions, but the necessity to insert a fairly stout needle into every muscle examined is a disadvantage. The instrument is most valuable in certain difficult cases and is essential for research work. In practice, the chronaximeter designed by Bauwens gives accurate information in the majority of cases, costs much less, and any number of muscles can be examined without damage to the skin. This apparatus is likely to supersede the customary examination by means of faradic and galvanic batteries.

DOSAGE OF RADIANT HEAT AND INFRA-RED RAYS

Although radiant heat and infra-red rays are perhaps the most widely used agents in electrotherapy and are recognized as effective therapeutic agents, little attention has been given to determining the optimum dosage. The important researches of Mayneord and Tulley (1943) have demonstrated serious defects in the design of heat lamps and cradles. Owing to distortion of the field of radiation by imperfect reflectors, "hot spots" in the generating elements and other factors, great variation occurs in the amount of energy absorbed by the part of the body under treatment. Using apparently identical technique at consecutive treatments, the dose absorbed by the tissues irradiated may vary by as much as 400 per cent. Mayneord and Tulley have designed a practical dose-meter and suggested a scientific unit of dosage. This is an advance comparable to the introduction of a standardized unit

of measurement in X-ray therapy, and it is to be hoped that comparable clinical progress will now be made in thermotherapy

PHYSICAL EDUCATION AND REMEDIAL EXERCISES

In the past, there has been an arbitrary distinction between physical education and remedial exercises. It is now realized that disablement of part of the body by disease or injury is accompanied to a greater or lesser degree by deterioration of the body physique as a whole. Thus exercises to remedy a local defect must be combined with general exercises to restore physical well-being and the ability to perform the customary work of the individual. The teaching of physical education is directed now, not only towards maintaining physical fitness, but also to detecting and remedying local defects or substandard general physique. The establishment of physical development centres and convalescent (rehabilitation) depôts in the Services, as well as the introduction of physical training instructors into Service and E M S hospitals, has led to a great improvement in the methods of maintaining and restoring physical fitness. Modern exercises are designed with greater regard to anatomical and physiological principles as well as being better adapted to the needs of individual patients. At the same time as the physical educationalists have been giving more attention to medical gymnastics, the physiotherapists, always expert in localized remedial exercises, have extended the use of general reconditioning to the early stages of recovery.

Thus recent years have seen the development of harmonious team work between physiotherapists and physical educationalists. This provides for the continuous restoration of function from the earliest passive or assisted movement in bed, through to the recovery of maximal capacity for work and recreation.

The pioneer work of Guthrie Smith (1943) in sling and pulley exercises has culminated in the development of compact and transportable apparatus consisting of a metal framework and a set of slings which support and facilitate movement in the whole or selected parts of the body. Using the slings, graded tension springs and weights, effortless movement or assisted and resisted exercises can be given to any joint and muscle group in the body. This apparatus supplies most of the advantages of exercise in water, is much cheaper and equally convenient to use in the ward, out-patient department or home.

OCCUPATIONAL THERAPY

It is becoming widely recognized that many of the psychosomatic complications of sickness and injury can be minimized by returning patients to work at the earliest possible moment. In many cases patients can return to modified work in their own trade long before they are fit to resume normal work. When practicable, the most beneficial type of occupational therapy is that which provides useful work within the capacity of the disabled person, carrying the normal trade wage and performed under industrial conditions, preferably with the patient's own firm. Research work in industry has revealed that there are ample jobs for all except the most severely handicapped, but the problem is to fit particular patients into the right job. This has led to the development, in a number of progressive firms,

of remedial workshops under industrial medical officers. Close liaison with the hospital treating the patient is essential and is exemplified by the scheme operated by the Austin Works and the Accident Hospital at Birmingham.

In many cases the nature of the illness and hospitalization prevent the use of the factory remedial workshop. Nevertheless, it is recognized that the early resumption of purposeful activity has a beneficial effect upon patients in hospital. Thus bedside occupational therapy has taken on new importance and is no longer termed "diversionary" but "general remedial therapy," in contradistinction to "local remedial therapy." The latter implies the use of craft-work to restore function to a disabled part of the body. There has been criticism of the light handicrafts, such as weaving, basket and leather work, commonly used in hospitals on the grounds that patients soon become bored. It is considered by many that the work, even in hospital, should be as nearly related to the normal work of the patients as possible and should carry the incentive of financial reward. This view has led to attempts to develop light assembly work in hospitals, but these attempts have not been altogether successful.

The consensus of opinion is that the light handicrafts are most suitable for the mixture of labourers, technicians, clerks and housewives in hospital and the arrangements should be made to transfer treatment to the appropriate industrial remedial workshops as early as is practicable. The light handicrafts are regarded as hobbies especially adapted to provide remedial exercise in an interesting form and essentially part of medical treatment. Patients are usually allowed to keep what they make on paying for the cost of the materials used, but there is no encouragement to work for profit. On the other hand, in the industrial remedial workshop financial reward is used as a stimulus to recovery, since the patient usually starts at less skilled work, possibly for short hours, and does not draw a full wage until back at his normal job.

Technical developments in occupational therapy have been in three directions. First, craft analysis, to which Kersley (1942), Haworth and Macdonald (1944) and others have contributed, which selects the appropriate craft to encourage particular movements—it is the basis of local remedial therapy in the hospital occupational therapy department. Secondly, job analysis which aims at fitting disabled persons into jobs within their capacity in industry. Thirdly, the development of handicrafts to meet the needs of all types of patients.

INFANTILE PARALYSIS.

The Kenny method—For the past ten years there has been controversy over the theories of the pathology and treatment of anterior poliomyelitis propounded by Kenny (1937). As the result of critical examination and research into her theories the majority of workers do not accept the views put forward by Kenny, but some notable support has been forthcoming. Most workers are agreed that Kenny has promulgated some useful therapeutic suggestions, especially in the use of frequent hot packs for the relief of pain and spasm as well as by advocating re-education movements at an earlier stage than had been the general custom. The controversy has served to draw attention to the need for greater medical supervision and more

thorough treatment in the convalescent stage. Most workers have re-affirmed the accepted principles of treatment by means of rest, warmth and splintage to prevent deformity in the febrile and painful stage, efficient re-education and adequate splintage to relax paralysed muscles during the convalescent period, and the value of stabilizing operations and efficient appliances for permanent deformities.

RHEUMATISM AND ALLIED DISORDERS

The past decade has been associated with substantial progress in the study and treatment of the so-called rheumatic disorders. The first step was the classification of the large number of clinical conditions labelled "rheumatism" by the medical profession and the public alike. There is now clear distinction between infective rheumatism (rheumatoid type arthritis and subacute infective non-articular rheumatism) on one hand, and chronic degenerative rheumatism (osteoarthritis and fibro-muscular degeneration) on the other hand. At the same time, the true pathology has been recognized of a number of clinical syndromes previously included in the "rheumatic" group, such as retropulsion of the intervertebral discs, industrial fatigue and occupational strains as the source of muscular and ligamentous pain. The etiological significance of psychogenic factors, faulty body mechanics, fatigue, focal sepsis and metabolic disturbance is appreciated more clearly.

Increased knowledge of the basic pathology has been followed by rationalization of the therapeutic measures. Thus infective rheumatism is treated by rest, measures to raise the general resistance, heat for the relief of pain and gentle movements to prevent stiffness. Degenerative rheumatism requires modification of the domestic and occupational habits of the patient, to provide more rest for the deteriorating tissues, combined with physiotherapy to relieve pain and maintain maximal function. Postural and occupational strains require a period of rest followed by active rehabilitation to restore the local and general physique. The use of local infiltration of novocain for diagnostic and therapeutic purposes has been a notable advance, as has also been the application of X-ray therapy to the treatment of ankylosing spondylitis. Greater accuracy in diagnosis and the introduction of some alternative therapeutic measures have reduced the empirical use of physical treatment, and this has been followed by general improvement in technique in the many cases for which physical treatment is the rational therapy of election.

References

- Bauwens, P (1941) *Proc roy Soc Med*, 34, 459
 — (1941) *Ibid*, 34, 715
 — (1943) *Ibid*, 37, 25
 Haworth, N A, and Macdonald, E M (1944) "The Theory of Occupational Therapy," London
 Kenn, E (1937) "Infantile Paralysis and Cerebral Diplegia," Svdney
 Kersley, G D (1942) *Brit J phys Med indust Hyg*, 5, 133
 Mayneord, W V, and Tulley, T J (1943) *Proc roy Soc Med*, 36, 411
 Smith, O F G (1943) "Rehabilitation, Re-education and Remedial Exercises," London
 Weddell, G (1943) *Ibid* 36, 513

INTESTINAL INFESTATIONS

By E H VERE HODGE, CIE, MD, FRCP (Lieut.-Col., IMS Ret.)
Lecturer in Diseases of Tropical Climates, University of Edinburgh

HOOKWORM DISEASE

THE prevalence of helminthic infestations has been, and will be, further increased with the return of soldiers from tropical areas and active service conditions, and it will be necessary to extend medical diagnosis, largely by clinical laboratory methods, to include certain infections hitherto familiar mainly to those working in the tropics. Of these, the most important is hookworm infection, usually of the species *Ancylostoma duodenale*. Many men have already returned carrying this infection, but in a light degree and showing only minor evidences of ill-health, the cause of which may be overlooked or, what is more common, ascribed to repeated attacks of malaria which may be coincident. *Ankylostoma* was formerly indigenous in the British Isles, hitherto the distribution has been confined to certain mines, notably in Cornwall, but it is not anticipated that the influx of persons carrying the parasite will cause any serious outbreak, as climate and sanitary conditions are inimical to the survival of the larvæ. Nevertheless, the parasite survives for five years and infected soldiers after discharge, widely scattered throughout the community, will require detection and treatment.

Infection is picked up from contaminated ground from which the larvæ penetrate the skin and entering the venules pass through the lungs and finally settle in the lower part of the duodenum, the jejunum and upper part of the small intestine where they attach themselves to the mucous membrane and suck blood. It is generally considered that the worm excretes any toxin but that the resulting symptoms are due to mechanical irritation and the draining of blood. There will be of two types—anæmia, characteristically with the fall in the hæmoglobin in advance of that in the number of corpuscles and depending in intensity upon the weight of infection and the amount of available iron in the food, and, secondly dyspepsia, sometimes suggestive of duodenal ulcer but more commonly associated with gaseous distension of the small intestine. Intermittent diarrhœa is a frequent symptom.

Diagnosis—Hookworm disease may be suggested by the anæmia and by eosinophilia variable in degree but not bearing any relation to the intensity of the infection. The diagnosis is confirmed by the discovery of ova in the stools, some process of concentration by centrifugalization or flotation is necessary, and the stools should be examined on several successive days.

Treatment—The effective anthelmintic drugs for this infection are carb tetrachloride and tetrachlorethylene. The latter is preferred as being less toxic and equally effective. The patient may experience a sensation of giddiness, drowsiness or even exhilaration, but toxic phenomena need not be anticipated with therapeutic doses. It is of advantage to combine this drug with oil of chenopodium, as this to some degree supplements the tetrachlorethylene and at the same time will remove any ascaris infection which is commonly coincident.

The patient should not be starved, but should receive a light evening meal, and in the morning, fasting, the following mixture —

Tetrachlorethylene	60 minims
Oil of chenopodium	16 minims
Saturated solution of magnesium sulphate	2 ounces

This dose is suitable for an adult, that for children being in proportion to weight

The solution is well shaken and prepared immediately before use. If there is no evacuation after four hours, a further dose of saline is given. Food may be taken as soon as the bowel is satisfactorily cleared. This treatment should remove from 80 to 90 per cent of the worms. A second course may be given for final eradication, but not before ten days have elapsed. Occasionally still further courses are required.

During the use of these anthelmintics, alcohol should be avoided for twenty-four hours before and forty-eight hours after ingestion. This particularly applies to carbon tetrachloride, which is dangerous for the use of alcoholic subjects or those with liver damage.

Full doses of iron complete the treatment

ASCARIS LUMBRICOIDES

Although this species is common in the British Isles, the load is usually light and not to be compared with the heavy infestations which may be acquired in tropical countries, notably in South China, where night soil is directly applied for the fertilization of vegetable crops. The ova are usually swallowed with contaminated food, but there is evidence that they may be dust-borne. The larvæ, set free in the stomach and upper intestine, having entered the blood stream, normally pass to the lungs, where they burst into the alveoli, causing, in heavy infections, petechial hæmorrhages or scattered areas of consolidation, which, becoming confluent, give rise to a condition known as ascaris pneumonitis. Aberrant larvæ may be carried to the brain, spinal cord or other organs, setting up local signs. It may be the larvæ, rather than the adult forms, which cause repeated convulsions in children. Finally, the maturing worms come to rest in the small intestine. Symptoms excited by the presence of the adult worms in the small intestine are variable. A small number may provoke severe symptoms, especially in young children, whilst a host may carry a comparatively heavy load, perhaps of thirty or more worms, and remain unaware of their presence. Symptoms are more likely to be severe if dead or dying worms are retained, as it is in this condition that the maximum amount of toxin is liberated.

Symptoms — The most common result of ascaris infection is a vague dyspepsia with loss of appetite and recurrent colic. Allergic phenomena, notably asthma, are produced in some cases. Periodically, cases are recorded in which the worms have provoked an intussusception or, becoming tangled together, have caused intestinal obstruction. The liability to this is increased by the use of unsuitable anthelmintics which disturb the worms without expelling them. For this reason, when treating any form of intestinal worm infection, it is desirable to start by expelling the *Ascarides*, should their presence be suspected.

Diagnosis may be automatic, the worms may be passed in the stools or vomited. This is particularly liable to occur during high fever. The ova may be discovered

in the stools by direct microscopic examination or preferably after concentration by dilution of the stools and centrifugalization. This method obviously will fail if the infestation consists, as sometimes happens, of a small colony of males. Detection is sometimes possible by the examination of the pattern of a barium meal in the small intestine. Eosinophilia is inconstant and is more likely to be high during the stage of larval invasion after a heavy infection.

Treatment—The anthelmintic generally found most effective and convenient is hexylresorcinol, administered in enteric-coated capsules, the adult dose being 1 gramme. The patient is given a brisk purge the day before, and a light evening meal. The drug is administered on an empty stomach, purgation commonly follows but a further saline purge may be given four hours after, if necessary. The dose may be repeated on the following night if the first has been unsuccessful and some authorities advocate a repetition daily for one week.

Maplestone (1934) regards oil of chenopodium as the most effective drug in this infection (cf. treatment of ankylostoma) and safe unless the patient is unduly debilitated. The usual dose is 1 minims for every year of age up to 16 minims. The drug is unsuitable for children under two years of age. Maplestone, however, advocates a larger dosage, three capsules each containing 10 minims at intervals of one hour, followed by a saline purgative after half an hour. Santonin, 3 grains with calomel 1 grain for an adult, is usually effective but may require repetition.

ENTEROBIUS VERMICULARIS (Syn *Oxyuris* THREADWORM PINWORM)
The importance of this worm lies in its extreme infectivity, the difficulty of eradication and the tendency to produce serious digestive and nervous symptoms or vaginitis. Although in many instances apparently healthy children have been found to be infected, the liability is usually due to a subnormal state of health. The worm is not infrequently found within the lumen of the appendix, but evidence as to its influence in producing appendicitis is conflicting.

Clayton Lane (1944) has given a comprehensive summary of the present state of knowledge. The parturient worm passes through the anal sphincter and deposits chains of eggs on the peri-anal skin or clothing, to which they are at first adherent. Once dried, however, the eggs become air-borne and have been recovered from the dust of sleeping rooms, especially if crowded. Thus, in addition to digital infection or auto-infection, air-borne infection is likely to occur. Although the life of the adult worm is less than a month, family or community infection may persist indefinitely unless the infection is eradicated from all carriers.

Diagnosis may be made accidentally by the discovery of the minute, thread-like worms in the stools, but a more detailed examination is usually necessary. Search for ova in the stools is likely to be fruitless, as they are seldom deposited within the bowel. They may best be collected with the aid of the cellophane swab. The "N I H" swab consists of a glass rod with rounded tip, covered with a square of plain non-waterproof cellophane and fitted in a test tube. The swab is firmly stroked over the peri-anal skin and the cellophane transferred to a slide, moistened with water or $\frac{N}{10}$ sodium hydroxide solution, for microscopic examination. The most productive time for the search is immediately the subject has risen in the morning.

Treatment—Wright and Brady (1940), after a series of experiments, concluded

at gentian violet, administered in enteric-coated tablets, is the most effective vermicide for this infection. The dose for adults is $\frac{1}{2}$ grain three times a day and for children $\frac{1}{4}$ grain for each year of apparent age, this is given in divided doses, thrice daily. They found the drug most effective if given in a water-soluble capsule designed to disintegrate in the small intestine four-and-a-half hours after ingestion. Two courses of eight days are given, with a seven days' interval between. A small proportion of patients suffered from nausea, vomiting, diarrhoea and abdominal pain, but these effects passed off quickly if the dose was reduced or omitted for a day or two. Stress was laid on the importance of detecting and treating all infected members of a family at one time. The drug is contraindicated in concomitant roundworm infection or cardiac, renal, hepatic or gastrointestinal disease. Treatment may be reinforced by enemas of soap and water or infusion of quassia to remove dead or dying worms.

Miller and Einhorn (1944) reviewed the symptomatology in two hundred patients. They found gentian violet, administered in enteric-coated pills twenty minutes before meals for two periods of eight days with a seven days' interval, the most effective form of treatment. In the case of young children unable to take the tablets an enema of 2 to 3 ounces of strong infusion of quassia, followed after 15 minutes by a soap and water enema, and given on alternate days for two months, was found effective. The usual measures against digital re-infection were taken.

Hexylresorcinol (see ascaris), given by mouth and supplemented with enemas of a solution of hexylresorcinol crystals of 1 per cent, retained for fifteen minutes, has given good results (*Brit med J*, 1944).

Pakenham-Walsh (1944) reports methylene blue, in doses of 3 grains three times a day for a week for an adult, as effective.

Phenothiazine has received trials but has been abandoned on account of toxicity.

TRICHURIS TRICHIURA (Syn *Trichocephalus trichiurus* WHIPWORM)

Small numbers of the ova of this parasite are frequently discovered during the search for ova of other species and the adult worm is sometimes seen. *Trichuris* inhabits the cæcum and, in spite of the fact that the head is attached to or penetrates the mucous membrane, little disturbance is caused by light infections. These worms are resistant to the ordinary anthelmintics.

Faust (1939) suggests that for persons harbouring heavy loads, tetrachlorethylene, 5 minims, or 3 minims per year of a child's age, after careful clearance of the bowel, is effective.

TAPEWORM

The only tapeworm to any extent prevalent in this country is *Tænia saginata*, the beef tapeworm. This is a comparatively harmless parasite and in many cases arouses no suspicion of its presence until segments are passed in the stools. In young subjects, digestive disturbances may be provoked and there may be evidence of malnutrition. The treatment is as described below for *T. solium*.

Tænia solium as an infection of endemic origin is of extreme rarity in this country, as pig infection is practically non-existent, but in other countries, notably

in India, the infection is common. The adult in the intestine may be equally innocuous with *Tænia saginata* but there is a liability to an alteration in the life cycle, so that the cysticercus stage properly belonging to the alternate host, the pig, develops in man. This may take place when the ova are ingested with contaminated food and water, by the carrier of an adult worm infecting himself by his fingers or by the regurgitation of gravid segments into the stomach. The larvæ set free in the stomach penetrate the tissues and cysticerci develop in any part of the body, especially in the muscles and brain. The graver symptoms are caused by the deposit of cysts in the brain, with resultant generalized or focal lesions. McArthur (1933-34) drew attention to the incidence of epilepsy due to cysticercosis of the brain among soldiers returning from India.

Dixon and Hargreaves (1944) have collected 284 cases (now increased to over 300) from Service sources. They record in detail the methods of diagnosis adopted, these include a thorough examination of the whole body for palpable cysts, with biopsy, if discovered, and radiological examination. The latter includes study of the whole body and will not reveal cysts unless they are calcified, a process which will take at least five years. Eosinophilia is found in 10 per cent of cases only. Casoni's intradermal test and the complement fixation test have been abandoned, as they have been found to be negative in high infestations.

Treatment is unsatisfactory and any attempt to destroy the cysts by anthelmintics is calculated to precipitate the appearance of symptoms, as these only arise after the death of the cysts. Surgical treatment for the epilepsy of cysticercosis has in no case relieved the symptoms.

Treatment of adult tænia—Liquid extract of male fern is an efficient expulsive but the routine of treatment must be observed rigidly and it may be necessary to repeat. After two days of minimal fluid diet with a daily saline aperient, 90 minims of the drug are given in soft gelatin-coated capsules, divided into three doses at intervals of half an hour. Dosage for children is calculated from the above dose for adults in proportion to body weight. Some three hours afterwards a further saline aperient is given. Castor oil should not be used as the toxicity is thereby increased. The patient remains in bed during treatment.

Andrews and Ogilvie (1944) reported the removal of four scolices from an adult patient, after three failures in seven months, with the following treatment—First two days fluids only and magnesium sulphate $\frac{1}{2}$ ounce in the morning. Third day sodium bicarbonate, 180 grains in water, followed thirty-five minutes later by 90 minims of liquid extract of male fern and finally magnesium sulphate $\frac{1}{2}$ ounce, half an hour later. They attribute this success to the undivided dose and to the sodium bicarbonate.

Houghton (1943) insists on sixty hours' complete starvation before final treatment. This regime, however, is not suitable for delicate subjects or children.

Mukerji and Maplestone (1943) consider carbon tetrachloride the most efficient anthelmintic in tapeworm infection. The full dose of 45 minims shaken up in 2 ounces of a saturated solution of magnesium sulphate is given and the usual precautions in the use of this drug observed. It should not be used until any coincident ascariis infection has been removed. They found tetrachlorethylene and hexylresorcinol to have expulsive action also but in definitely less degree.

HYDATID DISEASE

This disease is commonly regarded as of somewhat rare incidence in this country, and among cases recorded a proportion have contracted the infection abroad Wolfe (1943), however, points out that between 1926 and 1938, thirty-four patients were treated in Cardiff Royal Infirmary and that in a period of five years up to 1935, 103 deaths were recorded in England and 35 in Wales, the latter country therefore showing a higher incidence in proportion to the population. The condition is comparatively common in the Shetland Islands. Barrett and Thomas (1944) record that a number of cysts have been revealed by mass radiography and that such cysts remain silent unless infected. Roberts (1943) confirms Wolfe's findings and records two cases of cysts in the brain occurring in Wales. Punch (1939) describes the successful treatment of a patient with a cyst in the lung, by lobectomy.

Confirmation of *diagnosis* is obtained from Casoni's skin test, which gives positive reaction in 90 to 95 per cent of cases. Care, especially in dealing with children, must be taken in regulating the dose, as severe local and general reactions are liable to occur. The complement fixation test is recorded as positive in 80 to 95 per cent. Eosinophilia is not usually provoked unless there is leakage from a cyst, nor is the Casoni reaction.

TRICHINIASIS

Since the outbreaks in 1940-41 at Wolverhampton (Sheldon, 1941, Jolly, 1941), Hertfordshire (Garrod and Maclean, 1941), Penrith (Beeson, 1941), Birmingham (Bacon, 1941), and S E London, there appear to be no fresh records. In the reports on these incidents, stress was laid on the absence of symptoms of the invasion stage, that is, of vomiting and diarrhoea and on the early appearance of oedema of the eyelids, headache, fever and cough. Eosinophilia may not start for a week and is highest at the end of three weeks (Della Vida and Dyke, 1941). Andes *et al* (1940) report that eight persons in whom the diagnosis was made within three days of the onset of symptoms were cured completely and immediately with tetrachlorethylene. In each case there was a history of eating inadequately cooked pork from one to three days before the onset of symptoms, consisting of headache, malaise, abdominal discomfort, fever and oedema around the eyes.

PROTOZOAL INFECTIONS

In addition to *Entamæba histolytica*, described in part I of this symposium (p. 220), there are certain protozoal infestations of probable clinical significance.

GIARDIA LAMBLIA inhabits the duodenum and small intestine. It is recovered from the stools of infected persons. Recovery of giardia from the gall-bladder has been recorded by Hartman *et al* (1942).

The organism is frequently associated with chronic diarrhoea and there is still divided opinion as to whether it should be regarded as the cause or whether the altered character of the intestinal contents favours multiplication. With the introduction of mepacrine as a suppressive it has been possible to reassess the effect of this infestation, and records are accumulating of the clearing up of chronic diarrhoea, and even of certain cases of steatorrhoea, after removal of the parasites. It appears definite that giardia is not a cause of dysentery. The habitat is in the small intestine, and although giardia have been detected in the scrapings from ulcers of the amebic type, further search has revealed also *Entamæba histolytica*.

Katsampes *et al* (1944) suggest that giardia infection seriously interferes with the absorption of vitamin A, and probably other fat-soluble vitamins, in children.

Welch (1944) reports that after radiological examination, evidence of functional and anatomical changes in the duodenum, duodenal cap, pylorus and prepyloric area of the stomach was found in three-quarters of the series.

Treatment—The administration of mepacrine 0.1 gm thrice daily for three days clears the infection.

For children the doses suggested are —

1 to 4 years	0.05 gm twice daily
4 to 8 years	0.05 gm thrice daily
8 to 12 years	0.1 gm twice daily
12 + years	0.1 gm thrice daily

Infants under one year should not be treated.

Giardia, however, has been recovered from the stools of men who have recently ceased taking suppressive mepacrine in malarious areas. This and the discovery by Macqueen (personal communication) of giardia in the stools of a patient who was treated for the infection eighteen days previously suggest that mepacrine does not totally eradicate the organism, or that a fresh infection is easily contracted.

TRICHOMONAS HOMINIS, an active motile organism sometimes found in the stools, is generally regarded as harmless, although there would seem to be little doubt that heavy infections may give rise to an intractable diarrhoea of the small intestine type. No known drug is effective in clearing the infestation, although the effect of medication is apt to be misleading owing to the tendency of the parasites to appear in the stools in tides or showers.

References

- Andes, J. E., Greene, R. A., and Breazeale, E. L. (1940) *J. Amer. med. Ass.*, **114**, 2271.
 Andrews, G. W. S., and Ogilvie, A. C. (1944) *Brit. med. J.*, **1**, 772.
 Bacon, L. J. (1941) *Ibid.*, **2**, 909.
 Barrett, N. R., and Thomas, D. (1944) *Brit. J. Tuberc.*, **38**, 39.
 Beeson, P. B. (1941) *Proc. roy. Soc. Med.*, **34**, 585.
Brit. med. J. (1944) **1**, 445.
 Davis, E., and Allot, E. N. (1941) *Lancet*, **2**, 396.
 Della Vida, B. L., and Dyke, S. C. (1941) *Ibid.*, **2**, 69.
 Dixon, H. B. F., and Hargreaves, W. H. (1944) *Quart. J. Med.*, **13**, 107.
 Faust, L. (1939) "Human Helminthology," London, 374.
 Garrod, L. P., and Maclean, D. (1941) *Brit. med. J.*, **1**, 240.
 Hartman, H. R., Kayser, F. A., and Comfort, M. W. (1942) *J. Amer. med. Ass.*, **118**, 608.
 Haughton, S. (1943) *Brit. med. J.*, **2**, 380.
 Jolly, R. H. (1941) *Proc. roy. Soc. Med.*, **34**, 593.
 Katsampes, C. P., McCoord, A. B., and Phillips, W. A. (1944) *Amer. J. Dis. Child.*, **67**, 189.
 Lane, C. (1944) *Lancet*, **2**, 511.
 McArthur, W. P. (1933-34) *Trans. R. Soc. trop. Med. Hyg.*, **27**, 342.
 Maplestone, P. A. (1934) *Ind. med. Gaz.*, **69**, 266.
 Miller, J. F., and Einhorn, N. H. (1944) *Amer. J. Dis. Child.*, **68**, 376.
 Mukerji, A. K., and Maplestone, P. A. (1943) *Ind. med. Gaz.*, **78**, 282.
 Pakenham-Walsh, R. (1944) *Lancet*, **2**, 612.
 Punch, A. L. (1939) *Brompton Hosp. Repts.*, **8**, 150.
 Roberts, A. (1943) *Lancet*, **2**, 88.
 Sheldon, J. H. (1941) *Ibid.*, **1**, 203.
 Welch, P. B. (1944) *Gastroenterology*, **3**, 98.
 Wolfe, H. R. I. (1943) *Lancet*, **1**, 795.
 Wolfe, H. R. I. (1944) *Lancet*, **2**, 861.

ALLERGY

By DAVID HARLEY, M.D., B.Sc., F.R.I.C.

From the Laboratories of the Inoculation Department, St. Mary's Hospital, London

THE study of allergy continues to be an intriguing confusion of conflicting theories and rich promises. Much of this is due to ignorance of the fundamental principles involved, and also to the multiplicity of terms employed for the various types of allergic phenomena and to the different interpretation of the same term by clinicians and pathologists. Freeman's well-known story of the indignant doctor from Ohio, who came all the way to a "Congress of Allergy" in London in order to pour forth his views on asthma, and then found to his disgust "only Frenchmen and Germans talking about tuberculosis," is a case in point.

The search for an effective universal or non-specific desensitizing agent—of which peptone and autohæmotherapy were among the early claimants—continues. To the list of glorious failures must now be added diethylene sulphonate. Not quite in the same category has been the expenditure of a quantity of penicillin by American workers to demonstrate that, like the sulphonamides, it has little effect in uncomplicated asthma. Histamine-azoprotein, although it has not fulfilled its earlier expectations in asthma and rhinitis, gives some indication of being a valuable therapeutic agent in certain types of contact dermatitis.

Especially marked in the study of the allergic diseases has been the amount of labour expended in "debunking" new treatments. As Faraday more eloquently expresses it —

"The Truth of Science has ever had not merely the task of evolving herself from the dull and uniform must of ignorance, but also that of repressing and dissolving the phantoms of her imagination."

The psychological factor, active in the etiology of the allergic diseases, plays a definite part in the response of the patient to treatment, and for this reason allergy has been an exceedingly happy hunting-ground for the experimental therapist. That the enthusiasm of the originator of a new treatment is often the chief, or indeed the only, active factor in that therapy, is suggested by the excellent results obtained by the originators of new treatments and by the progressively poor results reported by later, and perhaps more sceptical, workers.

It is worthy of note that there has been an increase in the number of patients presenting themselves for treatment of allergic complaints during the past year. Especially noticeable have been those patients—usually women approaching middle age—with relatively slight asthma, rhinitis, or urticaria, often of several years' duration, who have reported a recent worsening of the condition. This may have been associated with the increase of the stress and strain of life during the last, and perhaps the most trying, winter of the war. In this connexion the psychologists' expression "escape from reality" seems to me perhaps not inappropriate, although I must confess to an ignorance of its precise meaning. Be this as it may, there is no doubt that there has been a sharp rise in the incidence of industrial contact dermatitis, which coincided with the increase of industrial activities to war-time level. The introduction of new industries and processes involving the

The principle of the test is the establishment of prolonged contact between the suspected allergen and the non-abraded epidermis

In the case of solids, a small portion of the powdered substance (which may be moistened) is placed directly on the skin, in the case of fluids, a small square of linen, gauze, or filter paper soaked with the fluid is used. The site is then covered with a larger square of cellophane or oiled silk, which is held by means of an overlapping square of adhesive tape. It is advisable to include a control test of cellophane or oiled silk with adhesive tape in case the patient is sensitive to these. Generally speaking, it is best to test on areas of skin fairly close to the dermatitis area, or on sites which have been involved in previous attacks although many workers routinely employ the skin on the back. The patches are left in situ for twenty-four to forty-eight hours, unless the presence of marked itching or a spreading rash demands their earlier removal. In the case of dress materials, and such-like, it is often necessary to leave the patch for seven to ten days before a reaction develops. This is probably due to the fact that the element of friction, often active in the natural induction of the dermatitis, is not duplicated by the method of testing, so that more prolonged contact is necessary. A positive reaction consists of a circumscribed area of inflammation, varying from erythema in the case of mild reactions to vesiculation with necrosis in the case of powerful allergens, and it often reproduces the type of lesion present in the patient.

Although the patch test has been established on its merits as a valuable diagnostic aid in allergic contact dermatitis, it is subject to the same limitations as those governing the dermal tests in other types of allergic disease, and the results must be interpreted with care and with due respect to the other aspects of the case.

BACTERIOLOGICAL METHODS IN ALLERGY

Pathogen-selective culture—This technique was originally introduced by Sobel Cohen as a selective method of culture for chronic infections in which the primary infecting organism tends to get crowded out with secondary invaders, e.g., colitis and the chronic dysenteries, and in bronchiectasis, and in which the routine methods of bacteriological culture frequently fail to isolate the primary infecting organism. The principle of the method is the utilization of the *in vitro* bactericidal power of the patient's blood to kill off the secondary invading organisms and those to which the patient is "immune," and to allow the growth of the potent pathogens. The technique is not difficult—

A small amount of the infected material is placed in a sterile 4 by $\frac{3}{8}$ inch test tube, which is then added 1 or 2 c cm of the patient's whole fresh blood, in the case of heavily infected material, such as sputum and faeces, it is better to make three or four serial dilutions of the material in blood in case the primary implant would prove too heavy, the tubes are incubated for twenty-four hours at 37° C. Subcultures are then made on to blood agar or other suitable media, and incubated. The resulting growths are examined, and compared with a control series of direct cultures of the pathological material.

BACTERIAL SENSITIZATION

By the term bacterial sensitization is meant those examples of the "hereditary allergy" group (asthma, rhinitis, urticaria) in which an infective factor appears to be of prime etiological importance.*

This is an aspect of the subject which seldom receives the attention it undoubtedly deserves, and it may be of moment to examine the reasons for this. It is impressive to witness the large percentage of asthmatic and rhinitis patients presenting their

* In this sense bacterial sensitization is of course quite distinct from allergy group "bacterial allergy," in which the allergic phenomena are usually side accompaniments of a systemic infection, e.g., the tuberculin reaction in tuberculosis.

cases for investigation, in whom the symptoms first appeared after, or in association with, some infective process—often comparatively mild infections of the respiratory tract, although it must be noted that a bacterial sensitization may occur in the absence of the usual signs of an acute or chronic infection. Most of these patients give negative or only feeble skin reactions to inhalant and food allergens, but bacteriological examination, employing pathogen-selective methods, almost instantly reveals abnormalities. The satisfactory results of desensitization with autogenous vaccines in these patients supports the hypothesis that the relationship between the bacteria and the asthma is one of cause and effect. However, it must be admitted that the precise nature of the mechanism by which the infective process produces the asthma or the rhinitis is by no means clear at present. The use of vaccines and bacterial extracts for diagnostic skin tests in such cases has proved unsuccessful.

Routine determinative bacteriological methods, in those cases in which the causal mechanism is a bacterial sensitization, are of little more use than would be the employment of routine toxicological methods in a case of food allergy. Now often are asthmatic patients seen in whom specific desensitization has failed and in whom "vaccines have been tried and found useless," when a subsequent trial with vaccines prepared by pathogen-selective methods gives excellent results. Partly to blame is the use of intradermal skin tests, which frequently give false positive reactions—in the absence of evidence of clinical sensitivity—that are liable to be misinterpreted by the enthusiast who considers all allergic patients in terms of skin reactions alone. The "vaccines have been tried" patients are usually those in whom the vaccine in question has been the product of a postal specimen sent to a commercial laboratory with the request "please make vaccine." This is about on the same level as sending a day's rations from a patient with suspected food allergy and saying "please make extract for desensitization treatment." When an adequate bacteriological examination employing pathogen-selective methods is not practicable, a good stock vaccine of appropriate type is much better than an "autogenous vaccine" made from a postal specimen by a technician in a laboratory divorced from clinical contact with the individual patient.

The majority of cases of chronic urticaria and angio-neurotic oedema occurring in adults appear to be of the bacterial-sensitization type—from an intestinal focus.

TREATMENT

The chief lines of specific treatment remain (1) avoidance, and (2) desensitization, with which must be included the use of pathogen-selective vaccines. The general principles of treatment are well known, and have already been reviewed elsewhere (Harley, 1942).

"*Relief of the toxic load on the colon*"—This rather old-fashioned outlook should be revived—in spite of academic doubts about the possibility of establishing sour milk bacilli in the intestine. The allergic patient with a streptococcal gut flora—whether or not the blood sedimentation rate be raised or excess indicanuria be present—nearly always obtains benefit from a course of lactic milk, with or without moderate use of colon lavage. The Express Dairy Company's "yoghourt" is—

will prove impressive, and it is reasonable to suppose that if physical education had been given its proper place in the general education of the child, the number of candidates for physical development centres would have been materially reduced. Evidence in support of this belief is to be found in the excellent results which have been obtained at these centres as the result of carefully graduated exercise.

PHYSICAL EDUCATION AT SCHOOL

With these facts in mind it is worth considering what is the value of physical education in the schools, and what part it should play in the general education of the child. It seems clear that an education which neglects the training and development of the body in its endeavour to educate the mind can never be entirely satisfactory. Training of the body and training of the mind should go hand in hand, the one incomplete without the other, there should be a constant ratio between the two. It is unnecessary to err on the side of exaggeration, physical education must take its position relative to other events and duties of life, but it is abundantly evident to those with experience of the young recruit that neglect of the physical side of education can be responsible for considerable mischief. It is sometimes argued that a good intellect can thrive in a sickly body. This may be true for the very few, but for the average person a sickly body usually indicates an ill-functioning mind, and for the majority a good physical condition will undoubtedly assist the efficient working of the brain.

Apart from these considerations there is another problem to which attention must be paid. There will always be a certain number of children whose intellect will never be of the first order, who will have to earn their living by manual work and rely on their muscles rather than on their minds. For these children, physical fitness is an even greater necessity, it is the nation's duty to do everything possible to develop the physically immature.

RESULTS OF PLANNED PHYSICAL EDUCATION

What can be expected of planned physical education carried out by fully trained physical educationalists? Broadly, the results that can be hoped for are as follows —

- (1) A healthy child will be maintained in good health
- (2) The physical make-up of the under-sized and under-developed child will improve
- (3) Faults of posture of body or feet will be corrected at or near their onset.
- (4) The child should get an appreciation and understanding of physical fitness which will persuade her to make every effort to maintain it in adult life.

The following arguments can be produced for believing that physical exercise will help maintain the health and improve the efficiency of the child —

- (1) Correct body carriage and correct ways of walking and sitting will allow the internal organs to function to their best advantage, and will also ensure economy of effort. A body in a state of equilibrium is well balanced and only the minimum of effort is required of the individual to maintain it in the erect position. When any part of the body is out of alignment the

muscles which keep it erect are constantly at work, and this entails fatigue

- (2) Muscular movements do not consist solely of muscular acts, in the first place they are carried out by the concentration of the higher centres, they are therefore as much a nervous as a muscular process and have a stimulating effect, not only on the muscles but also on the mind. It is also not generally recognized that fatigue during exercise is often exclusively fatigue of the central nervous system and not of the muscles performing the act. These aspects of physical exercise are frequently overlooked.
- (3) The respiratory and circulatory systems have their part to play in exercise, eight to twenty times more oxygen is needed during physical work than at rest, and the burden of meeting these demands falls on the heart and lungs. Any picture of physical exercise must therefore include the whole range of these activities.
- (4) When the movements of the body become coordinated there is increased economy of effort, every day exercise is carried out with a minimal expenditure of energy, and correct habit paths are formed. With repetition of movements or training, a harmony of action of all parts of the body is achieved, clumsiness disappears and there is finally no sense of effort.
- (5) There is no doubt that well-planned physical exercise can produce a sense of well-being which reacts on the individual as a whole, and colours her relations with other people, the teacher should consider it part of her duty to convince the pupils, from their own sensations and from observations of each other, that this is in fact true.
- (6) There is finally a social and æsthetic value in a good carriage and appearance of well-being, which is a valuable asset in all walks of life and should not be underestimated. An opinion regarding a person's character and mental attitude can be formed from her posture, and may decide whether she will make a satisfactory employee or not. Claims are also made that exercise is intimately related to mental, moral and social training, this may well be the case, but such effects are difficult to assess, except over long periods, and this article is concerned only with results directly observed.

THE MEDICAL ASPECTS OF PHYSICAL EDUCATION

part from the aspect of physical exercise which deals with the healthy child or the maintenance of positive health, exercise can also be used as a medical or medical agency. In the schools, the disabilities treated by this means will be mainly faults of posture of the body and feet, these, in the early stage of their development, can be entirely remediable, but if allowed to become a habit, present more difficult problem. It is most desirable that this work should be carried out in the school, the saving of time alone for the child and the adult who will accompany her to the hospital or outside clinic is worthy of consideration. In addition to this, the fact that the treatment is carried out by someone familiar to the child, who will continue to observe her in normal class work, is a definite advantage.

SUGGESTED REGIME FOR SCHOOLS

The type of physical exercise to be carried out in the school must be determined by the physical educationalist together with the physical medicine specialist and the much debated point whether or not it should be made a compulsory part of education in all types of schools must also be decided. In connexion with this latter, it is difficult for the uninitiated to understand why, if the general curriculum as carried out in the school is accepted without question as the practice of the school, the physical side of the education should not also be an integral part of the general routine. So far as the type of physical exercise is concerned, from the medical point of view it should be designed to achieve some, if not all, of the following aims —

First, the child should be taught to sit, stand and walk correctly, and it is of primary importance that these acts should become as natural and automatic as other routine acts of life. The lesson can best be demonstrated in front of a mirror and when the child is of a suitable age she should be made to appreciate the æsthetic advantage of good poise and posture.

The movements should be bilateral in order to develop the body symmetrically; every part of the body should be exercised and the time-table should, so far as possible, be made up of free natural movements carried out through their full range. The body should be kept pliable and elastic, and alertness and quickness of action should be cultivated. Every time-table should include periods of relaxation, both of separate parts of the body and of the body as a whole.

Exercise should be capable of modification and adaptation to suit the varying needs of children of both sexes and all ages, and no hard and fast rules should be laid down, if under the direction of fully trained physical educationalists, this should be quite practicable.

Music for some of the movements gives enjoyment, helps relaxation and gives an opportunity to teach rhythm. It is also restful, as it does not involve the constant attention and consequent fatigue of unforeseen movement.

Much can be learnt from the physical exercises as carried out in the A.T.S. they in large measure achieve the aims set out above, but in making this suggestion it must be made quite clear that the exercises designed for the women in the Army are entirely unrelated to militarism.

Conditions under which physical exercise should be carried out and the ideal for the standard of frequency should be determined, and every effort must be made to keep to the programme. Half an hour's exercise daily should be aimed at; failing this, three-quarters of an hour three times a week, one long session a week must be discouraged. When suitable, classes should be held in the open air, but in bad weather a light airy room is necessary, large enough to allow freedom of movement. In cold weather the room should be warmed, since cold tends to produce spasm in the muscles and defeats the object of the exercise. The floor when possible, should be of non-splintering wood in order that some exercises can be taken bare-foot. Mirrors are a valuable part of the equipment—no lesson is more telling than one learnt by direct observation of oneself.

Army physical training has shown that apparatus is not essential for enjoyment and good results, but where apparatus is available it should not be used to the

exclusion of free standing exercise. The size of the class should be limited to one which makes it possible for the teacher to observe every child. Finally, it is of great importance that the classes should excite interest and pleasure. Dull and heavy exercise will create a dislike for physical work, it will only be taken under compulsion, and the aim of developing, and enjoyment of, exercise for its own sake will be defeated.

DIET AND ENVIRONMENT

A final, but most essential, consideration is the importance of good nourishment, proper hours of sleep, and good social conditions, if a child is to benefit from the physical side of its education. It has been shown that lack of fat tissue and firm muscle development makes the maintenance of good posture more difficult. There also seems no doubt that an ill-nourished child, or a child suffering from insufficient or disturbed sleep, cannot benefit from, or take part in, physical exercise with such zest as can a healthy child. During this war, regular mid-day meals and daily milk have been the established routine in many areas, this service should be extended to all schools where there is the need. Every effort should be made to improve housing conditions and to educate the public as to the importance of hygiene, proper hours of sleep, fresh air, and regular habits, in this the medical officer, the physical educationalist and the social worker or Care Committee worker must combine together as a team.

THE POST-SCHOOL PERIOD

In conclusion, if physical education is satisfactorily established in schools throughout the country it must also be made possible for its continuance after the school period. There is evidence that the first four to five years after leaving school are the most testing, physically, for the young adult, because of the complete alteration in his or her mode of life. For the boy or girl, work in the shop or factory will mean a change from an existence which has on the whole been regular and organized, during which there have been considerable periods spent in the sitting position, and for a certain proportion, regular meals and hours of sleep. The new mode of life often means long hours of standing, not always under good hygienic conditions and, for many, irregular and unsuitable meals. In addition, there are all the attractions of cheap ill-fitting shoes and clothing, and of a new-found liberty to pass their leisure time without the experience which will enable them to use it to good purpose. There should be adequate medical surveillance during this period, and arrangements must be made for carrying out remedial treatment for errors of posture of body or feet which give rise to symptoms. There should also be provision for all workers to get well-balanced mid-day meals at a reasonable cost, and ample facilities must be given for physical exercise and all forms of physical recreation.

PRACTICAL NOTES

THE DANGERS OF THE EXTERNAL USE OF THE SULPHONAMIDES

THE following points are culled from a Report of the Council of Pharmacy and Chemistry of the American Medical Association (*Journal of the American Medical Association*, August 4, 1945, 128, 1024). Although the frequency of reactions from the external use of the sulphonamides is difficult to assess, it is obviously considerable. One investigator, for instance, reports sensitization in 5.5 per cent of 218 minor surgical patients treated with a 5 per cent sulphathiazole cream. The type of cutaneous reaction varies greatly from a local fixed reaction to exfoliative dermatitis. In addition, there is the complication of photosensitization. Relapses are not uncommon, and involvement of the scalp may result in temporary loss of the hair. "The therapeutic value of the sulphonamide compounds is well established, but they are undoubtedly often being used carelessly for skin lesions. Their use on the skin for ordinary skin disorders should be frowned on. Other measures should be employed first, then if local sulphonamide therapy is necessary it should not be continued for a period longer than five days, because of the danger of sensitization of the patient. Such therapy should be employed only under a physician's direction." The Report draws special attention to the possible dangers in paediatric practice, such as the possibility of harmful results following the routine use of suspensions of sulphonamides for the prevention of impetigo in nurseries.

ANÆSTHESIA IN THE AGED

IN an article dealing with the subject of choice of anæsthetic for the aged or elderly patient, Surg. Lieut.-Commr. E. H. Watts (*Canadian Medical Association Journal*, July 1945, 53, 20) draws attention to the need for a thorough investigation of the cardiovascular and respiratory systems and the state of the kidneys. Another factor to be borne in mind, which directly affects the choice of drug for pre-medication, is that of apprehension, owing no doubt to a subconscious idea that awakening may not take place after anæsthesia. If morphine must be employed in the presence of pain the dose should be light, rarely more than 1/6 of a grain. Atropine, in dosage up to 1/100 of a grain, and hyoscine, in dosage up to 1/150 of a grain, both control secretion and stimulate the basal centres, and, in addition, the latter drug produces a high degree of amnesia and good

sedative effect. The barbiturates are respiratory depressants, but in the case of a local block spinal anæsthesia they are most valuable, maximum dose for an elderly patient, however, should be 1½ grains of nembutal, or a comparable dose of other selected drugs. As regards choice of anæsthetics, although age and sex have been given as contraindications to the use of intravenous pentothal sodium, supplemented by nitrous oxide and oxygen, this methoxanæsthesia is stated to have proved to be a useful and excellent combination. In an aged patient the dosage should be initially very small, supplemented with small fractional doses repeated more frequently, if necessary. In any case respiratory depression will not be a cause for concern. Cyclopropane possesses advantages of rapid and smooth induction, rapid recovery and excellent relaxation, allowing the use of high oxygen concentrations. Following its irritating effect on the lungs, liver and kidneys, it is steadily decreasing in favour of elderly patients. Nitrous oxide is useful for minor operations, but there is always the danger of anoxæmia. Chloroform should not be used for elderly patients, unless its use is rendered compulsory by lack of other agents, as in common practice. Recognition of the value of continuous spinal anæsthesia for the elderly patient is growing. Here, again, proper support measures are necessary. The author states that the dosage need never be high at any given time if initial massive dosage is employed, one of its main advantages is completely lost. Initial massive dosage of single administration results in high absorption and reactions. If this is avoided the patient need never have a large amount of the drug employed to de-toxify at a later time. Another advantage of this method is that the dosage can be made to conform to the case. Using Lemmon's technique (*Ann. Surg.*, 1941, 131, 141) working against time is eliminated and additional doses can be given if more time is required for the operation.

CLINICAL HÆMOGLOBINOMETRY

AS a result of numerous criticisms of direct hæmoglobinometers in use in the Glasgow Royal Infirmary, A. Brown (*Glasgow Medical Journal*, August 1945, 144, 39) investigated the calibration of twenty hæmoglobinometers of the Sahli type. It was found that 100 per cent of these instruments corresponded to a range of 10.4 to 17.0 grammes of hæmoglobin per 100 c.c. of blood. In other words, a normal

100 c.cm. might give a reading of anything from 88 to 144 per cent. depending upon the instrument used, whilst an anæmic blood with a hæmoglobin concentration of only 11 gm per 100 c.cm. might give a reading of 106 per cent. Within such a range of instruments the normal colour index would need to be regarded as 0.88 to 1.44. Three colour standards supplied for use with Sahli instruments were found to be an unsatisfactory match for any commonly used pigment in any dilution, in daylight or in artificial light. It is therefore recommended that a standard of reference should be adopted in nœglobinometry and that this should be the oxygen capacity of blood, the hæmoglobin level being expressed in grammes per 100 c.cm. of blood. The expression of hæmoglobin concentration as a percentage of "an arbitrary and often unknown 'normal'" is strongly deprecated. In collaboration with A. Bruce Anderson the same worker (*Ibid*, 144, 44) has correlated the results obtained with a photo-electric colorimeter calibrated in volumes per cent of oxygen capacity with the actual oxygen capacity of the samples of blood taken, and has found that this instrument gives an accurate measure of the oxygen capacity of the blood within the limits investigated, i.e., a hæmoglobin content of 6.6 to 16 gm. per 100 c.cm.

holding the solution to be aerosolized. A safety valve in the lid allows the internal pressure to be varied from 8 to 50 lb. The rapid passage of the steam creates a vacuum in the tube, allowing the aerosolized solution to be drawn up and sprayed from the nozzle in a fine mist mixed with steam which can be safely inhaled six inches from the spout. A special screw valve controls the rate of flow, so that a given amount can be aerosolized in any given length of time. The 16 ounces of water are used up in twenty to twenty-five minutes. The absence of water automatically shuts off the current.

Preliminary studies showed that with sulphadiazine (2.5 gm in 50 c.cm. water), blood levels of 5 to 12 mgm. were attained in half an hour and maintained for four to six hours. In the case of penicillin, the findings in two patients treated with 180,000 units were that the blood level increased from 0.5 unit penicillin in half an hour to 2.12 units by the first hour, a level of 1.05 units being maintained for three hours subsequently. In the fifth and sixth hours there was still 0.128 unit per c.cm. of serum.

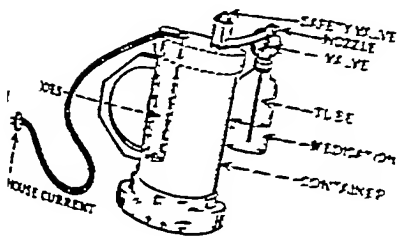
THE ESTIMATION OF PEPSIN IN GASTRIC CONTENTS

The increasing importance attached to gastric analysis lends interest to a simple method of estimating the pepsin in gastric contents which is described by I. S. Kleiner (*Journal of Laboratory and Clinical Medicine* Jul 1945, 30, 624). It is based upon the milk-clotting action of gastric juice, and, a adult human gastric juice contains no rennin, a measure of the milk-clotting power is a measure of the pepsin.

(A) Solutions are required for the estimation of pepsin which is made by dissolving 42 gm. of NaOH in about 500 c.cm. distilled water, adding 115 c.cm. 60 per cent acetic acid, and diluting to 1000 c.cm. This solution keeps well. (B) Fresh cow milk. Equal volumes of A and B are mixed well, 10 c.cm. of the mixture being required for each estimation. The estimation is made as follows:—The gastric contents are centrifuged or filtered, if necessary. The reaction to Litmus, Congo red, if used, if acid, 1 c.cm. of gastric contents is diluted to 50 c.cm. with water and mixed well. If not acid, a small amount is diluted separately, with an equal volume of 1% HCl, mixed well and then diluted 1 c.cm. to 25 c.cm. with water. A test tube containing 10 c.cm. of distilled milk is placed in a water bath at 20°C. One c.cm. of the acid gastric contents is added to the test tube, quickly mixed and the water bath removed. The mixture is then mixed with the water bath removed. The mixture is then mixed with the water bath removed. The mixture is then mixed with the water bath removed.

A NEW AEROSOLIZER

Recent work on aerosols indicates that there will be an increasing demand for aerosolizers. Most models so far described have been too expensive for use on a large scale. Interest therefore attaches to a new simple model described by S. J. Prigal and F. D. Spear (*Bulletin New York Medical College*, April 1945, 8, 21). This consists of a container which holds 16 ounces of water suspended



from the lid into the water. The electrical contact begins to emerge from the spout, which is designed to allow a small bubble of steam to pass over a fine glass tube. The container

is then placed in a water bath at 20°C. One c.cm. of the acid gastric contents is added to the test tube, quickly mixed and the water bath removed. The mixture is then mixed with the water bath removed. The mixture is then mixed with the water bath removed. The mixture is then mixed with the water bath removed.

NOTES AND PREPARATIONS

NEW PREPARATIONS

DICOUMARIN (3 ¹-methylene-bis-(4-hydroxy-coumarin) is a synthetic anticoagulant for the treatment of thrombosis and embolism and their prevention post-operatively. It is issued in tablets of 50 mgm, in containers of 25, 100 and 500, price 9s 6d, 32s 6d, and 145s, by Ward, Blenkinsop & Co Ltd, Brooklands, Halewood, Liverpool, who have also placed on the market **MENAPHTHONE** and **ACETOMENAPHTHONE**, synthetic analogues of vitamin K, prepared for the treatment and prevention of conditions of hæmorrhagic diathesis associated with hypoprothrombinæmia. Menaphthone is supplied in ampoules containing 5 mgm menaphthone dissolved in arachis oil, in boxes of five 1 c cm ampoules, price 5s each, and acetomenaphthone in bottles of 25 and 100 tablets of 10 mgm, price 3s and 10s 6d, respectively. Literature relating to these products is available on application to the manufacturers.

ROYAL MEDICAL BENEVOLENT FUND
CHRISTMAS GIFTS

In his appeal letter this year Sir Arnold Lawson writes—

"The Christmas Gifts appeal has a special significance this year, for although peace has come, the material blessings which peace is supposed to bring are as yet merely dreams without substance. Food is monotonous and scarce; fuel is terribly short and its cost fantastic; clothing and prices generally are on the same high level and even for those in fairly comfortable circumstances the outlook for the festive season is distinctly drab. Inevitably the burden of high prices and shortage falls most heavily on the poor and for them there will be little money for celebrations of any sort this coming Christmas.

The sum collected last year was a record one—£1,817—and 483 beneficiaries received a gift of £3 each, and 184 of the poorest a further gift of £2 for the New Year. A still better response is hoped for this year, so that, if possible, each beneficiary may receive £4, and the very poorest an extra £1. The sum total needed to achieve this aim is £2,000. In Sir Arnold Lawson's words—

"Is it too much to ask? A very generous profession has already done so much, but my excuse is the hard times which still lie ahead. Believe me, the gratitude these Christmas Gifts evoke is very great and often extremely moving."

Donations, marked "Christmas Gifts," should be sent to the Secretary, Royal Medical Benevolent Fund, 1 Balliol House, Manor Fields, Putney, S W 15.

NATIONAL BABY WELFARE COUNCIL

The National Baby Welfare Council has issued a useful pamphlet on the subject of measles, which covers the onset

rules to be observed during the period, menstruation and pregnancy, after delivery, during breast feeding, and at the time of the menstrual pause. Copies, price 2d each or 1s 9d per dozen, can be obtained from the Secretary, National Baby Welfare Council, 29 Gordon Square, London, W C 1.

THE MEDICAL USE OF THE
SULPHONAMIDES

The second edition of *The Medical Use of the Sulphonamides* (Med Res Coun War Med No 10), by various authors, edited by J. Hawking and F. K. Green, contains a useful section on penicillin and its relation to the sulphonamides. From among the various new sulphonamides and related drugs which have been produced and tested since the first issue of this monograph in 1943, sulphamerazine, phthalylsulphathiazole and marfanil have been selected for inclusion in the new edition, which is obtainable from H M Stationery Office, price 1s 3d.

WELLCOME MEDICAL DIARY 1946
Owing to paper shortage a limited number only of the 1946 edition of the Wellcome Medical Diary can be printed, but practitioners who have not sent in their request for a copy are invited to apply to Burroughs Wellcome & Co., 18 Fuston Road, London, N W 1.

CHANGE OF ADDRESS

MESSRS HOUGH, HOSEASON & CO LTD, Manufacturing Chemists, have moved to more commodious premises, and as from September 1, 1945, their address will be Chapel Street, Levenshulme, Manchester, 19.

CONTENTS FOR DECEMBER, 1945

DISEASES OF THE BLOOD

- The Diagnosis of Anæmia* By John F. Wilkinson, M.D., F.R.C.P., F.I.C.
The Treatment of Anæmia By Harold Fullerton, M.D., M.R.C.P.
Anæmia in Childhood By Ursula Shelley, M.D., M.R.C.P.
Purpura By S. C. Dyke, D.M., F.R.C.P., D.P.
Infectious Mononucleosis By Sir Henry Trueman, M.B.E., M.D., F.R.C.P.

Health XVIII—The Control of Infectious Fevers of Childhood By C. M. Smith, D., D.P.H.

THE DIAGNOSIS OF ANÆMIA

By JOHN F WILKINSON, M D, PH D, F R C P, F R I C

Physician and Director, Department of Clinical Investigation and Research, Manchester University and Royal Infirmary, Manchester

THE diagnosis of an anæmia should normally offer little difficulty provided that the picture has not been obscured by previous treatment with combined liver, iron, or vitamins, which are so often given before a diagnosis has been made, this is deprecated, since correct or satisfactory assessment of the type and character of the blood dyscrasia may thereby be completely prevented.

Anæmia may be due to (1) acute or chronic blood loss following injury, continuing or intermittent hæmorrhages from the alimentary or genito-urinary tracts, or in association with hæmorrhages due to abnormalities of the blood and blood vessels, such as hæmophilia, telangiectases and the purpuras, (2) hypoplasia or aplasia of the blood-forming tissues, as occurs in aplastic anæmia, agranulocytosis and thrombocytopenic purpura, (3) excessive red cell destruction, as in the acute and chronic hæmolytic anæmias, due to abnormalities in the blood or the red cells, toxic or infective factors, and in some cases to unidentified causes, (4) defective blood formation, as in the deficiency anæmias, which include the two large groups of megalocytic and microcytic anæmias, respectively (Wilkinson, 1936).

Although a particular sequence of symptoms may be associated with any one of these anæmias, it must be appreciated that the development and severity of the symptoms will vary considerably in different patients according to, among other things, the age and sex, the causative factor, the rapidity of onset of the disease, and the severity of the blood changes. Thus, anæmia may develop so insidiously that considerable physiological compensation may mask its presence until quite a late stage and a patient may have been working up to the time of examination with a red cell count of $1\frac{1}{2}$ millions or less, whilst many a housewife has carried on satisfactorily with a hæmoglobin of less than 30 per cent. On the other hand, a different and more rapid mode of onset may lead to marked symptoms of anæmia in a patient with considerably higher values than these.

ETIOLOGICAL FACTORS

From the etiological point of view many of the blood dyscrasias show well-defined features. Thus familial or hereditary tendencies are noted in the telangiectases, hæmophilia (in males), acholuric jaundice (a familial hæmolytic anæmia), and especially pernicious anæmia, whilst the leukæmias, neutropenic states, aplastic anæmia, chronic hypochromic anæmias, purpuras, and other hæmolytic anæmias are not. The age of onset may have diagnostic significance—pernicious anæmia most commonly begins over the age of forty-five, whilst achrestic anæmia may start at twenty to forty years, and the hæmolytic anæmias at any age. Chronic hypochromic microcytic anæmia is noted between the ages of twenty and fifty,

In pernicious anæmia, and less frequently in chronic hypochromic microcytic anæmia, recurrent soreness of mouth and tongue, frequently put down to smoking and often going on to ulceration and atrophy of the tongue papillæ, is a prominent feature rarely seen in other anæmic conditions. On the other hand, necrotic ulceration of the buccal and pharyngeal mucous membranes and fauces, without surrounding tissue reaction, but often with concomitant swelling of the neck suggests the presence of an agranulocytosis. Ulceration of the gums with purpuric manifestations and bleeding would indicate an acute leukæmia, whilst in the acute monocytic leukæmia a peculiar œdematous purple swelling of the gums resembles that seen in scorbutic patients. In aplastic anæmia, oral manifestations are rare in the earlier stages, but in the terminal stages of the disease there is nearly always bleeding from the gums, with or without epistaxis.

The *gastro-intestinal disturbances*, such as flatulent dyspepsia, particularly after meals, nausea, vomiting and loss of appetite, with constipation or looseness of the bowels, are all symptoms commonly associated with achlorhydria or achylia gastrica, and are therefore found in pernicious anæmia and achlorhydric hypochromic microcytic anæmia (Wilkinson, 1936). Dysphagia, like koilonychia, is an almost pathognomonic symptom seen in the so-called Plummer-Vinson syndrome of chronic hypochromic anæmia with dysphagia and achlorhydria.

Loss of weight may be marked in pernicious anæmia, but negligible in the achlorhydric hypochromic microcytic type, whilst in chronic leukæmias marked or little change may occur, gross splenic enlargement often counteracting any slight loss of weight.

Menstrual disturbances are common in chronic hypochromic anæmia and may be an important factor in its etiology, since it is a condition that is seen almost exclusively in women.

Neurological changes as a rule are seen only in pernicious anæmia, in which the early peripheral neuritis, with pins and needles, numbness and cramps in the limbs and cold damp feelings in the lumbar region, may later go on to postero-lateral sclerosis, but occasionally peripheral and central nervous system lesions may be observed when leukæmic processes or deposits involve or mechanically compress the spinal cord or peripheral nerves. Some patients with chronic hypochromic anæmia may complain of paræsthesiæ in the limbs. A Raynaud type of phenomenon with slight scleroderma or erythromelalgia in the lower limbs is sometimes noted in patients with polycythæmia rubra.

In the *cardiovascular and respiratory systems*, the clinical features seen are common to most of the anæmias with no particular diagnostic significance, manifesting themselves as dilatation of the heart, low blood pressure, sometimes rapid pulse, œdema of the ankles, generalized systolic murmurs, with dyspnoea and palpitation of varying degree.

Enlargement of the spleen may be found to a varying degree in many conditions such as polycythæmia, the hæmolytic anæmias, thrombocytopenic purpura, less often in pernicious anæmia, and still less frequently in chronic hypochromic anæmia. In Banti's syndrome with a mild non-specific anæmia the spleen may be enlarged before or after enlargement of the liver has been noted. In the chronic leukæmias, Gaucher's disease, Niemann-Pick disease, and Cooley's anæmia

especially of long standing, the spleen may be so much enlarged that the notch and right border may be on the right side of the abdomen with the lower pole in the pelvis, on the other hand, in certain acute, especially undifferentiated, leukæmias, the spleen may not be palpable at all on examination. It is important to remember that splenic enlargement may be one of the first signs of Hodgkin's disease or of subacute bacterial endocarditis with anæmia, and that it also occurs in conditions such as infective mononucleosis. Other conditions associated with enlargement of the spleen, such as malaria and many tropical diseases, may not be associated with any anæmia, but occasionally the institution of the specific treatment may lead to the development of anæmia or other blood dyscrasia.

Anæmia associated with *hepatic enlargement* is most commonly seen in Banti's disease, chronic cirrhosis of the liver and in chronic myeloid leukæmia.

Many other minor points of interest may be observed during examination of the patient; thus retinal hæmorrhages occur quite commonly in pernicious anæmia and in thrombocytopenic purpura, whilst optic atrophy has been noted from time to time in the former disease.

BLOOD CHANGES

The changes in the constituents of the circulating blood provide the most important evidence of the type of blood dyscrasia present, and diagnosis depends to a great extent upon these hæmatological determinations. Therefore before any anti-anæmic therapy is given, a full blood examination must be made, with particular reference to the red and white blood cells, hæmoglobin, differential white cell count, reticulocytes, platelets, red cell volume and fragilities, and van den Bergh reaction.

In this way important preliminary data are obtained, indicating either the correct diagnosis at once or a condition that requires further elucidation. Thus a megalocytic or high colour index anæmia will have a much diminished red blood cell count, often below 1 million per c mm., with reduction in hæmoglobin percentage, so that the colour index is usually greater than unity but on occasion may be a little less. With these changes it is usual to find in the peripheral blood variable numbers of nucleated red cells, especially megaloblasts and normoblasts, whilst the red cells may show irregularity in size and shape, polychromasia is often present.

Of this group, *pernicious anæmia* is the outstanding and most common member, but, as already discussed elsewhere (Wilkinson, 1936), a fault anywhere in the sequence of events in the gastro-hæmopoietic mechanism will lead to the same ultimate megalocytic blood picture, so that a clear idea of the site of failure is essential for correct diagnosis and treatment. The differential diagnosis from other megalocytic anæmias, such as achrestic anæmias, the acute hæmolytic anæmias, and certain rare but difficult early acute leukæmias, which closely resemble pernicious anæmia in the early stages, may require the help of other diagnostic procedures. Estimations of the daily reticulocyte count will show them to be at normal levels in a resting or non-remitting pernicious anæmia, only increasing temporarily under the influence of treatment or spontaneous remissions and then returning to normal after the maximum reticulocyte crisis has been reached on the seventh to tenth day; on the other hand, in the hæmolytic anæmias with severe megalocytic or normocytic anæmia, and often with megaloblasts and normoblasts in the peripheral blood, the reticulocytes remain high (10 to 30 per cent. or more).

necrotic ulceration of the mucous membranes, brawny swelling of the neck, glandular enlargement, moderate and non-specific anæmia, gross reduction in the number of white cells with few or no granular cells, no splenomegaly, a normal gastric acidity, a marrow showing absence of granulocytes, and no evidence of an bacterial factor

Thrombocytopenic purpura is associated with recurrent petechiæ or ecchymose in the skin and other tissues, hæmorrhages from any mucous membrane, and severe secondary anæmia with a much reduced platelet count, usually below 80,000 per c mm., prolonged bleeding time and poor clot retraction, and a normal gastric acidity, the spleen may be enlarged and the bone marrow shows very few platelets or megakaryocytes (Wilkinson, 1940)

The common features in the group of *hæmolytic anæmias* are evidence of a severe hæmolytic process and jaundice leading to a megalocytic or normocytic anæmia polychromasia, normoblasts and megaloblasts in the blood, high and persisting reticulocytosis, increased red cell volume, positive van den Bergh reaction and Schumm's test, normal gastric acidity, an enlarged spleen and an extreme normoblastic hyperplasia of the bone marrow. In acholuric jaundice increased red cell fragility will be seen but is not invariable. An accurate differential diagnosis of the anæmias in this group requires a careful consideration of these and many other clinical and etiological features

In *pernicious anæmia* there is a severe megalocytic anæmia, polychromasia, anisocytosis and poikilocytosis, reticulocytosis after treatment, frequently splenomegaly, achylia gastrica, whilst the bone marrow shows a typical megaloblastic hyperplasia, the patient may show a peculiar lemon-yellow colour of the skin, glossitis, flatulent dyspepsia, diarrhœa, paræsthesiæ or symptoms and signs of postero-lateral sclerosis

Achrestic anæmia is a severe anæmia resembling pernicious anæmia but the gastric acidity is normal, there is a variable splenomegaly, no neurological symptoms, a megaloblastic hyperplasia of the bone marrow, normal liver content of the anti-pernicious anæmia factor, and poor response to treatment

Chronic hypochromic microcytic anæmia occurs almost exclusively in women who complain of symptoms of a severe anæmia, flatulent dyspepsia, recurrent diarrhœa, soreness and ulceration of the mouth and tongue, koilonychia, often dysphagia and menstrual disturbances, splenomegaly is uncommon, the blood shows an anæmia with a very low colour index, achylia gastrica as a rule, a normoblastic bone marrow, no evidence of hæmolysis, van den Bergh and Schumm's tests negative, there is a rapid response to iron therapy

Acute leukæmias usually start as a severe megalocytic or normocytic anæmia, often resembling pernicious anæmia or hæmolytic anæmias with low total white cell count and nothing abnormal in the peripheral blood, a normal gastric secretion, van den Bergh and Schumm's tests negative, no reticulocytosis or evidence of hæmolysis, but bone marrow biopsy ultimately shows evidence of a leukæmic process, either myeloblastic or lymphoblastic in type, and then the typical blood picture follows, with hæmorrhagic manifestations

References

- Wilkinson, J. F. (1936) *Brit. Encyclop. med. Pract.*, 1, 407.
(1940) *The Practitioner*, 145, 382

THE TREATMENT OF ANÆMIA

BY HAROLD W. FULLERTON, M.D., M.R.C.P.

Department of Medicine, University of Aberdeen

It is obvious that accurate diagnosis of any disease should precede treatment, and it is justifiable to open this article with such a trite remark because in the æmias the proper sequence is often not observed. Most of the mistakes made in the treatment of anæmia can be avoided if less reliance is placed on clinical examination alone in the detection of anæmia and if a blood examination is carried out before the institution of treatment. Only too often is a patient judged to be anæmic by the pallor of his face, and he may then be subjected to troublesome and expensive treatment with liver extract or iron, or both. It should be realized more fully that a low hæmoglobin concentration in the blood is only one of several causes of pallor. The colour of the mucous membranes is a more reliable indication of anæmia, but even with considerable practice mistakes may be made. If anæmia is suspected, either from the symptoms or the physical signs, its presence and its severity should be determined by an estimation of the hæmoglobin concentration. To establish the type of anæmia present further investigations are necessary, the most important of which is examination of a blood film. This determines whether the anæmia is of the iron-deficiency type or whether it is dependent upon deficiency of the anti-anæmic factor of liver, as in pernicious anæmia. Iron and liver extract are the mainstays of treatment but they can be used intelligently only if the type of anæmia requiring treatment is first established.

One or two common misconceptions may now be mentioned. There exists a regrettable and rather widespread belief that liver extract is a specific for anæmia in general and not only, as is the case, for pernicious and allied anæmias. Another common fallacy is that liver extract enhances the effect of iron in simple iron-deficiency anæmia. One result of these errors is that a large proportion of the liver extract used is wasted and much needless expense and trouble are entailed. Another difficulty not infrequently encountered is when a patient is referred for blood examination for the first time after a course of liver extract parenterally and iron by mouth. In such circumstances it is often impossible to decide whether iron-deficiency anæmia or pernicious anæmia, or either, existed before treatment was started, and therefore the treatment which should be continued cannot be determined without observation for a considerable time.

IRON-DEFICIENCY ANÆMIA

By far the most common type of anæmia is one in which the red cells are small and poorly filled with hæmoglobin due to a deficiency of iron. It is very common in infants, especially in those of low birth weight and those who have suffered from infections. It is relatively rare in childhood and in adult males, but in women of reproductive age it is of frequent occurrence, although there is considerable evidence that the incidence has decreased during the war years (Davidson *et al*, 1944, Fullerton *et al*, 1944). The condition in women is due essentially to a chronic deficiency of iron which develops because the iron content of the diet is unable to compensate for the demands imposed by menstruation and pregnancy.

Accordingly, "chronic nutritional hypochromic anæmia" is a better name than "idiopathic hypochromic anæmia" or "simple achlorhydric anæmia." In addition a similar type of anæmia follows chronic loss of blood from any cause, for example hæmorrhoids, and develops after a severe acute hæmorrhage, such as hæmatemesis.

In all these circumstances the anæmia responds to iron therapy unless there is continuing loss of blood, or severe chronic infection. Iron must be given only by mouth, there exists at present no satisfactory preparation for parenteral use because, by this route, iron is toxic in doses large enough to correct anæmia. A choice is usually made between a ferrous salt, such as the sulphate, or one of the scale preparations, especially iron and ammonium citrate. The advantage of the ferrous salts is that the optimal dose is much less than that of the ferric salts of the scale preparations, 9 to 12 grains daily of ferrous sulphate stimulate hæmoglobin regeneration as effectively as 90 grains of iron and ammonium citrate. But ferrous salts in simple solution are somewhat rapidly oxidized to the much less effective ferric state, and therefore they are usually taken in the form of sugar coated tablets. Tab ferrous sulphate, 3 grains three or four times daily, is widely used in the treatment of iron-deficiency anæmia and has, to a considerable extent, replaced the iron and ammonium citrate mixture (30 grains three times daily) which held pride of place for many years. From the point of view of efficacy there is nothing to choose between them, but the advantages of convenience and low cost lie with the tablets. Several other preparations of iron are available but they have no real advantages over those mentioned. The use of elegant and expensive products containing both iron and liver extract should be deprecated, because, as stated above, liver extract has no effect in simple iron-deficiency anæmia.

Lack of response to iron—When iron is given in the doses mentioned to patients with iron-deficiency anæmia, blood regeneration proceeds rapidly, the hæmoglobin level usually increases by at least 1 per cent. per day and the sense of well-being which results is remarkable. If the hæmoglobin level does not rise satisfactorily, it is probable that chronic blood loss is occurring and careful investigations to discover its source should be made. In women, excessive menstrual loss is a common cause of failure to respond satisfactorily to iron, and it should be borne in mind that a woman's estimate of the severity of such loss has been shown to be unreliable in many cases (Fowler and Barer, 1935). Sometimes the induction of an artificial menopause by radium is necessary before the anæmia can be relieved.

In some rare cases iron-deficiency anæmia responds poorly to iron therapy, even in the absence of blood loss or the inhibiting effect of chronic infections. In such cases it is probable that absorption of the ingested iron is defective, and there is some evidence that this may be improved by giving ascorbic acid, in doses of 50 mgm. thrice daily, along with the iron. The powerful reducing action of vitamin C may facilitate absorption by increasing the proportion of the ingested iron which reaches the intestine in the ferrous state (Powell, 1944).

Intolerance to iron—Not infrequently, patients are seen who claim that all forms of iron cause nausea, vomiting and abdominal pain of such severity that the treatment has to be stopped. Cases of real intolerance to iron may exist, but I have never to meet a patient who is unable to take the drug in therapeutic doses if certain precautions are observed, although the discipline and encouragement available

only in hospital may rarely become necessary. Gastro-intestinal disturbances due to iron can be avoided in the great majority of cases if (1) the initial dose is small, say one-third of the optimal dose, and increases are made slowly, and if (2) the drug is taken immediately after meals and followed by a drink of water. In addition, it should be emphasized that gastric upset of this kind is, as a rule, only transient and will disappear after a few days.

Maintenance treatment—When iron-deficiency anæmia has been completely relieved, further treatment is unnecessary unless blood loss continues. Sometimes women are seen who can maintain a normal hæmoglobin level only if small doses of iron are taken regularly. In such cases the recurrent demands for iron imposed by menstruation are heavier than normal but not severe enough to justify the induction of a radium menopause.

Diet—As indicated above, one important factor leading to a negative iron balance in many women is dietary deficiency of iron. In most cases this is due to economic circumstances, since many foodstuffs rich in iron are somewhat expensive. The "bread and tea" type of diet commonly taken by women of the poorer classes is deficient in many respects other than iron and should be corrected as much as possible. Improvements which can be made without increased cost have been described by Davidson and Fullerton (1938). It should be noted that a diet rich in iron is not sufficient to correct anæmia once it has developed, medicinal iron is essential for this purpose.

PERNICIOUS ANÆMIA

Standardization of liver extract—It is now twenty years since Minot and Murphy discovered the remarkable effects of liver in pernicious anæmia and, although since that time much brilliant work has led to a new conception of the disease and to the provision of extracts of liver of high potency, the results of treatment in general cannot be regarded with equanimity. One reason for this is that despite much labour the chemical constitution of the factor in liver which induces remission in pernicious anæmia has not yet been discovered. Until this goal is reached clinical testing of liver extracts in patients in relapse is likely to remain the only means whereby the potency of extracts can be determined. Firms making liver extracts have enlisted the help of clinicians who are prepared to carry out such tests, but there is no obligation to do so, and sometimes suitable patients are scarce. As a result, inactive extracts appear on the market from time to time, and anyone who sees many cases of pernicious anæmia will have encountered several severe relapses, and perhaps deaths, due to this cause alone. In addition to this, however, another difficulty exists. In this country there is no indication of the degree of activity of extracts except the recommendations as to dosage provided by the manufacturers. The practitioner has therefore to choose a preparation without any real knowledge of the amount of the anti-anæmic factor it contains. Accordingly, it is gratifying to find that the question of standardizing liver extracts has received attention recently (Emery and Hurran, 1945). There is no doubt that clinical testing of extracts before they are issued should be made compulsory. In addition, some method of indicating the degree of potency should be established. The accuracy which can be achieved is probably not great, but the adoption of any method which gives even an approximate indication of concentration would be a

considerable advance In the United States, extracts must be tested clinically before being approved by an Advisory Board, and the Board assesses the potency of each extract in terms of "units" per c cm (A "unit" is that amount of an extract which, when injected daily, produces a satisfactory reticulocyte response and rate of red cell increase in at least three cases of pernicious anæmia) In Canada a somewhat similar method has been introduced

TREATMENT IN THE STAGE OF MODERATE RELAPSE—Most patients with pernicious anæmia when first seen have anæmia of moderate severity (hæmoglobin 30 to 50 per cent) but their lives are not in immediate danger In these circumstances the patient should be confined to bed until treatment has raised the hæmoglobin level to 60 per cent In this way undue strain of an enfeebled myocardium is avoided

The essential part of treatment is intramuscular injection of *liver extract* The many preparations available may be divided roughly into two groups—(1) concentrated and (2) crude extracts Generally speaking, the dose of a crude extract is double that of a concentrated preparation, but the potencies vary within wide limits and, for reasons stated above, no more accurate guide can be given Because crude extracts have not been shown to have any advantages over the concentrated ones in the treatment of Addisonian pernicious anæmia, a concentrated extract prepared by a reputable firm should be chosen A dose of 2 c cm, injected deeply into the gluteal region on each of the first two days of treatment, followed by 2 c cm once weekly, is sufficient to stimulate the maximal rate of erythropoiesis in the great majority of cases The weekly injection should be continued until blood examination gives results which are normal *in all respects* It is not enough to bring the hæmoglobin level to 90 per cent. or more, because macrocytosis may persist beyond this point When the red cell count is normal ($4\frac{1}{2}$ millions for women and 5 millions for men) and examination of a film shows no macrocytosis, the dosage may be reduced to maintenance levels

Iron—Although, as has been stressed, liver extract is not indicated in the treatment of iron-deficiency anæmia, iron is often necessary for a complete remission in pernicious anæmia, because, as large numbers of new red cells are formed, the available stores of iron may become exhausted In such circumstances, the hæmoglobin lags behind the red cell count as the remission progresses and a low colour index results This occurs most often in women between the ages of forty and fifty who probably have had some deficiency of iron before pernicious anæmia developed However, it is a good plan to ensure always a sufficiency of iron for full hæmoglobin regeneration by prescribing iron routinely, in the doses recommended above, for about a month.

SEVERE RELAPSE—Sometimes the practitioner is called upon to treat a patient in whom, for various reasons, the anæmia has become so severe that life is in immediate danger In such cases liver extract should be injected at once, but it must be realized that an interval of four to five days elapses before any beneficial effects can be produced The decision that has to be made is whether or not the patient is likely to survive this latent period without the help of blood transfusion This should be avoided in severe pernicious anæmia unless it is clearly evident that it constitutes the patient's only chance of survival, because in such cases the

ardium is the seat of marked fatty degeneration. Acute circulatory failure, manifested by acute pulmonary œdema and death, may follow the increased produced by blood transfusion. If it is decided that blood transfusion is sary, then ordinary whole blood should not be used but the concentrated sus- of red cells which remains after most of the plasma is withdrawn (Murray, and Shaar, 1943, Evans, 1943). In this way greater increases in the hæmo- in level following transfusion can be achieved with less risk of increasing the d volume too much and so precipitating circulatory failure. Now that blood ifusion centres prepare large quantities of plasma, such red cell suspensions ften discarded as a waste product. Experience has shown that they should always sed in preference to whole blood in the treatment of severe chronic anæmia. 'aintenance treatment—When the blood count has been restored to normal dosage of liver extract should be reduced. 2 c cm of a "concentrated," or m. of a "crude," extract every two or three weeks, is sufficient for most patients, a blood examination should be done at least once a year so that the dosage be increased if any signs of relapse appear. Treatment on these lines should tain the patient in perfect health and free from any risk of developing sub- e combined degeneration of the cord. Patients do not object to or neglect ntenance treatment if the necessity for it is explained to them, and practitioners id be more generally aware of the fact that relapse is inevitable sooner or later eatment is discontinued.

ALLERGIC REACTIONS TO LIVER EXTRACTS—Most practitioners have l experience of untoward reactions occurring a few minutes after the injection liver extract. They vary in kind and severity from flushing of the skin and cal urticaria to severe asthma and alarming collapse. Sometimes the allergic e appears to be transient and reactions do not recur with subsequent injections ey can usually be prevented by subcutaneous injection of a few minims of enaline at the same time as the liver extract is given, changing the brand extract is seldom successful. In some cases, however, reactions are severe and sistent, so that a choice has to be made between desensitization and changing oral therapy. A successful method of desensitization has been described by Sorley and Davidson (1944). If it is decided to stop injections, administration hog's stomach by mouth is probably the best alternative. Desiccated stomach P.C.) and such preparations as pepsac are usually required in a dosage of at est half an ounce daily for proper maintenance. They must not be heated, and ey have an unpleasant taste and smell which can be improved by exposing the ext day's dose to the air overnight in a saucer covered with muslin.

SUBACUTE COMBINED DEGENERATION OF THE CORD

This serious complication does not occur if the blood is kept normal by adequate maintenance treatment, it is particularly liable to develop in those patients who, as a result of insufficient treatment, have a subnormal blood count, e.g. Hb 70 to 80 per cent. and R.B.C. 3 to 3½ millions, over a considerable period. Once the con- dition has become established, considerable improvement may be achieved, parti- cularly in early cases, by massive doses of liver extract. This entails giving three or four times the doses recommended above for maintenance treatment, should be continued for at 12 months, even in the absence of n

In order to procure maturation of the embryonic red cells, which only occur in the red bone marrow in postnatal life, the individual must be supplied with a *maturing agent*. This maturing agent is derived from the mother's blood by the developing foetus and stored in its liver. During the first few weeks of neonatal life the infant uses this store to produce mature red cells. Later on, this agent is thought to be manufactured by the infant itself. This hæmatinic principle is formed by the interaction of an enzyme made by the gastric mucosa (intrinsic factor) and the extrinsic factor, derived from the protein part of the diet. If this maturing agent is not present, the immature red cells (megaloblasts) will enter the bloodstream, be dealt with as foreign bodies and rapidly destroyed. In addition to the hæmatinic principle the red cells need thyroxin, vitamin C, copper, iron and manganese for their perfect production. Of these, copper and manganese act to act as catalysts in the absorption of iron. Although most of the iron derived from the breakdown of hæmogoblin is retained in the body, some is lost. If this waste fraction is not replaced by ingestion of the metal, an iron deficiency anæmia results. Similarly, if thyroxin or vitamin C is deficient, anæmia will occur. The necessary amount of copper and manganese is absorbed together with the iron of the diet.

The *colour index* is a numerical expression of the hæmogoblin content of the individual red cell. If the cell value is 100 and the hæmogoblin content is 100, the colour index is 1. This index is used in some descriptions to differentiate between the various types of anæmias. In some of these, the iron deficiency type, the hæmogoblin is reduced more than the number of red cells, so that the colour index is much below 1. In pernicious anæmia, due to deficiency of the hæmatinic principle, the red cells are more affected than the hæmogoblin carrying power, so that the colour index is greater than 1.

TYPES OF ANÆMIA

(1) *Hypochromic anæmia* is one with a low colour index when the percentage of hæmogoblin is reduced to a greater extent than the total number of red cells. Example, the iron deficiency anæmia of artificially fed infants.

(2) *Hyperchromic anæmia* is one with a high colour index when the red cells are more reduced in number than in their hæmogoblin content, for example, pernicious anæmia.

(3) *Megalocytic anæmia* is one in which the red cells have a greater diameter than normal, for example, pernicious anæmia.

(4) *Microcytic anæmia* is one in which the red cells have a smaller diameter than normal, for example, iron-deficiency anæmia.

(5) *Erythroblastic anæmia* is one in which the primitive red cells are seen in the peripheral blood, for example, hemolytic disease of the newborn.

It is important to determine the cause of an anæmia, when possible, before starting on curative treatment or when trying to prevent anæmia.

Dameshek (1945) has pointed out that any anæmia may be caused by (a) deficiency of materials needed for blood production, (b) disturbance in the marrow, (c) increased loss of the bone marrow's finished product, the red cell, whether by hæmorrhage or by increased hæmolysis. This method of classification simplifies the nomenclature, makes the clinician consider the patient as a whole, and increases the chance that the treatment will be scientific rather than a "hit or miss" effort.

The causes of the various types of anæmia may be classified as follows —

- (A) DEFICIENCY
 - (1) Deficiency of iron
 - (a) Due to dietetic causes
 - (b) Due to prematurity
 - (c) Due to disorders of the alimentary tract
 - (2) Deficiency of the hæmatinic principle (pernicious anæmia factor)
 - (3) Deficiency of thyroxin
 - (4) Deficiency of vitamin C
- (B) BONE MARROW DISTURBANCES
- (C) EXCESSIVE BLOOD LOSS
 - (1) Due to acute or chronic hæmorrhage
 - (2) Due to hæmolytic processes
- (D) COMBINATION OF ALL THREE ABOVE
von Jaksch's anæmia

DEFICIENCY ANÆMIAS

(1) DUE TO DEFICIENCY OF IRON

(a) *Lack of iron in the diet* — Dietetic anæmias are common in infancy and somewhat less commonly encountered in childhood. The anæmia is hypochromic, the hæmoglobin being greatly reduced and the red cells less affected. The white cells are normal unless infection is also present. The anæmic child is otherwise healthy. There is no evidence that either sex is more affected than the other.

In breast-fed babies the anæmia appears between the ages of four and five months, and in artificially fed babies it is apparent between three and four months (Mackay, 1933). This anæmia occurs more commonly among the infants of anæmic mothers and reaches a lower hæmoglobin value in such cases. The onset is gradual, and the susceptibility to infection is usually the first indication that the baby's blood is abnormal. It is extremely difficult to assess an infant's degree of anæmia unless a blood count is done.

The cause of the anæmia is twofold — (1) depletion, during the first six months of extra-uterine life, of the stores of iron in the infant's liver derived from the mother during the last few weeks of intra-uterine life, (2) deficiency of iron in milk, this being more severe when cow's milk takes the place of human milk. Cause (1) explains the increased incidence of this type of anæmia in premature babies, in twins and in babies born of anæmic mothers. In later childhood, the anæmia commonly follows acute infectious fevers and disturbances of the gastro-intestinal tract, particularly when diarrhœa persists for several weeks. The hæmoglobin will also be lowered by acute and chronic hæmorrhage, especially when the economic level of life prevents the use of a good mixed diet during the convalescent period.

In 1943 Davidson *et al.* showed that children of five to twelve years attending municipal schools were more likely to develop this type of anæmia than children of other age-groups and of better economic standards. The anæmia then found was exaggerated only amongst this age-group during the war years of 1942-3.

Treatment — This anæmia will usually react favourably to intensive iron therapy, provided the causative factor is concomitantly treated. Brokaw *et al.* (1942) concluded from a series of observations on babies in a "well baby" clinic that the early addition of cereals, vegetables and eggs had no marked effect on the hæmoglobin level or on the red cells. Mackay *et al.* (1945) showed that the use of national bread, of iron medicated bread and of iron cooking utensils did not

appreciably raise the level of hæmoglobin in children from one to five years attending London day nurseries. It is advisable that iron mixtures should be given to infants from an early age, from four to six weeks in premature babies, from twelve to fourteen weeks in completely artificially fed babies, and from sixteen to twenty weeks in breast-fed babies. The iron may be given as the ferric salt in the form of iron and ammonium citrate, $1\frac{1}{2}$ grains three times a day, increasing to 10 grains three times daily, or as the ferrous salt in a mixture containing ferrous sulphate $1\frac{1}{2}$ grains three times daily, increasing to 6 grains three times a day. Individuals differ in their ability to take iron, one type of iron will produce diarrhoea quickly in some infants whilst another type may cause obstinate constipation. Either result will obviously interfere with the therapeutic response. In old children the same variations will occur and each case must therefore be treated as an individual. In older children, too, it is essential that the diet should be made interesting and that it should contain a high proportion of first-class protein together with food rich in vitamins. In addition to the iron mixtures mentioned there is a large assortment of iron-containing pills and mixtures on the market; it is urged that all practitioners should study the iron content of each recommended dose before prescribing these and waiting for a therapeutic response.

(b) *Prematurity as a cause of iron deficiency*—The physiological changes in the blood at full term are all exaggerated, the more premature the baby the more marked being the blood destruction. At birth, the hæmoglobin level is high and the red cells more numerous in the very premature baby and both are broken down more rapidly and their fall is greater. Consequently, their return to normal is slower (Mackay, 1933). Immature red cells are more common in the first weeks of life but they rapidly disappear after this to return again about the sixth week. The destruction goes on for about three months, during which time the greater fragility of the immature red cells accounts for their greater destruction.

Treatment with iron and liver has no effect. It appears to be impossible to prevent the condition, but the infant should be given full doses of vitamins, plenty of sunlight and fresh air, if strong enough to go out of doors, or doses of ultra-violet light if very frail. Should the anæmia show signs of becoming severe or should the baby contract any infection, a blood transfusion, using fresh blood of the appropriate group (10 to 20 c.c. per pound body weight) should be given without delay. Later, after the third month, the premature infant is particularly liable to an iron-deficiency anæmia of the hypochromic type. The causes of this are the low stores of iron in the liver, the greater liability of infection, and a relatively more rapid growth than in the full-term infant. Prevention of this late anæmia depends upon careful attention to the diet, which must include vitamins and mineral salts. Iron must therefore be added to the premature baby's diet from the age of four to six weeks. Fresh air should be allowed freely, but prevention against infection should be energetically carried out. When the anæmia has arisen, the curative treatment depends upon adequate doses of iron. Very small babies do not tolerate iron well, therefore it is best to go slowly at first, giving the iron mixture separately from the milk and immediately before the feeds. Best of all, iron should be given from the first few weeks, as advocated above. On the whole, these babies tolerate iron and ammonium citrate better than ferrous sulphate.

(c) *Chronic disorders of the alimentary tract as a cause of iron deficiency*—Such disturbances of the normal digestion as cœliac disease, chronic diarrhœa of a non-specific type and infestation with parasites, may so interfere with the absorption of dietetic iron from the irritated mucous membrane of the intestines that a low hæmoglobin anæmia may result. Similar malabsorption may occur from the disturbed mucosal lining of the intestines in rickets, sprue, vitamin C deficiency and mucous colitis, which is only found in older children. All these, except rickets, are uncommon. Non-absorption of iron will not affect the number of red cells but each red cell will be deficient in its hæmoglobin content, so that the type of anæmia found will be hypochromic with a low colour index.

Treatment consists in dealing with the primary disorder as well as giving full therapeutic doses of iron.

(2) DEFICIENCY OF THE HÆMATINIC PRINCIPLE (RED CELL MATURING FACTOR)

Pernicious anæmia or the megalocytic hyperchromic anæmia produced by this deficiency is so rare in infancy and childhood that it remains an enigma and its easy diagnosis suggests that insufficient study of the blood film or of the clinical picture has caused a mis-diagnosis. The condition, when proved, does not differ in essentials from that found in adult life. Treatment is also similar.

(3) DEFICIENCY OF THYROXIN

The hypochromic anæmia which is found in cretins and hypothyroidic children is nearly always associated with coincident infection, especially of the upper respiratory tract. The *treatment* depends upon removal of the infection, with replacement of thyroxin and adequate doses of iron. The thyroid medication must continue for a long time, if not for life, if the child is to remain in good health.

(4) DEFICIENCY OF VITAMIN C

Whether scurvy is latent or acute there is always some degree of anæmia. In the latent type, the child is always tired and disturbed by some intercurrent infection. Bruising or oozing from the mucous membranes may occur following trauma. The anæmia is mild, hypochromic, and of low colour index.

In the acute type, obvious signs of bleeding into the joints, subperiosteal areas, or from the nose, bladder, mouth or vagina, may occur. The anæmia may be severe, the red cells being reduced more than the hæmoglobin is, lowered.

Treatment consists in giving adequate doses of vitamin C, which will produce an immediate rise in the reticulocyte count. Iron alone will not improve the anæmia.

BONE MARROW DISTURBANCES

(1) *Aplastic and hypoplastic anæmia*—Toxins which depress the cell-forming powers of the red bone marrow are more dangerous but less easily detected in childhood than in adults. Secretions of pathogenic organisms, such as the *Treponema pallidum* and the hæmolytic streptococcus, are powerful depressants of the bone marrow function.

In addition to bacterial poisons other toxins may produce the same effect. Arsenical therapy for congenital syphilis, X-ray and radium treatment of skin diseases or malignant growths may cause such an anæmia. Sulphonamides may produce a similar result in some individuals. Lead may give rise to a hypoplastic

anæmia if children suck toys or nursery furniture painted with lead-containing paints. The anæmia of cretinism or hypothyroidism may be of this type, as was the more common hypochromic iron-deficiency anæmia. Chronic nephritis with urea retention, occurring later in childhood, may have a similar effect and cause the same blood picture.

All these causes may not only depress the red cell-forming function of the marrow but they will also destroy the finished product, the red cell itself. Thrombocytolysis may take place in the blood stream.

(2) *Displacement of the red bone marrow* itself by deposits of lymphosarcoma, leukæmias, multiple myeloma or other tumours, is extremely rare in childhood but should be borne in mind. All the organized bodies of the blood picture are decreased in number. The red cells drop steadily until they reach a figure of less than one million, but each red cell carries its full complement of hæmoglobin so that the anæmia is normocytic and normochromic. Hence the colour index is round about unity. The white cells and the platelets are also diminished. There are no immature cells at any time.

Diagnosis should be confirmed, when possible, by bone marrow biopsy, either by sternal puncture or trephine of a long bone.

Treatment depends for effectiveness upon the ability to remove the causative factor, for example, lead, hypothyroidism. The anæmia may be improved by blood transfusions and iron therapy. If the cause is irremediable, repeated transfusions will keep the patient alive for a varying period.

EXCESSIVE BLOOD LOSS

(1) *Due to acute or chronic hæmorrhage*—Anæmia obviously follows hæmorrhage from whatever cause, for example, after tonsillectomy, following injury (including trivial injuries in hæmophilia) or after bleeding from any orifice. The least well remembered, although probably the most common cause, of this type in childhood is that following acute hæmorrhagic nephritis. The insidious anæmia due to the constant loss from a bleeding rectal polyp is less commonly found. Hæmorrhage due to umbilical sepsis or to congenital abnormality of the bile duct may be overlooked owing to the interest of the primary lesion.

Treatment depends upon the arrest of the hæmorrhage, replacement of the blood lost, by fresh blood transfusions, and by iron medication until the hæmoglobin reaches a normal figure.

(2) *Hæmorrhagic disease of the newborn*—An additional type of bleeding which demands special mention, occurs within a few days of birth. This is called hæmorrhagic disease of the newborn. In this condition the bleeding is associated with a prolonged bleeding time, due either to a deficiency of thrombokinase (Barr, 1941), or to a deficiency of fibrinogen (Allibone and Baar, 1943), or most commonly to a hypoprothrombinæmia. This latter condition is then exaggerated by some form of trauma and resultant bleeding may occur. The cause of hypoprothrombinæmia is deficiency of vitamin K, which is normally converted by the liver into prothrombin. If the infant is premature, his liver will have stored very little vitamin K from the maternal sources, or if the mother's diet has been deficient she may have had too little vitamin to pass on to her child.

The bleeding occurs from any or several mucous surfaces, for example, melæna

umbilical stump, urinary or vaginal tracts. Blood may also extravasate subcutaneously, or hæmorrhage into the suprarenals may cause sudden death in the affected new-born baby. The bleeding may occur suddenly in an otherwise normal infant during the first four days after birth. It ceases spontaneously within the first week, if the baby survives. Mortality is less than 10 per cent. Prevention could be undertaken on a large scale if every mother were given an intramuscular injection of 1 to 2 c cm. of naphthoquinone or 2 c cm. of vitamin K during labour, preferably within six to eight hours of delivery. During the last few weeks of pregnancy a daily dose of 2 c cm. of vitamin K has also been shown to decrease the incidence of this disease. Some authorities further safeguard the infant by giving 0.5 to 1.0 mgm. of naphthoquinone within the first twelve hours after birth. It is best to give this by injection rather than by the mouth, because vitamin K causes quite severe abdominal colic when given orally.

Curative treatment depends upon giving the infant 0.5 to 1.0 mgm. of naphthoquinone as soon as possible after hæmorrhage occurs, if the baby has not already had a prophylactic dose. If bleeding begins in spite of an adequate dose of vitamin K, it is essential that a blood transfusion be given, for the hæmorrhage cannot be due to hypoprothrombinæmia. The baby must be kept warm, breastfeeding should be continued unless the bleeding is from the stomach, in which case oral feeding should be stopped for twelve hours. Fluids should then be given by intravenous, rectal or subcutaneous drip transfusion of one-fifth strength saline. If vitamin K is not available, the bleeding may be stopped by giving one, two or three intramuscular injections of maternal blood into the baby's thighs and buttocks, 10 or 20 c cm. may be given at a time, depending upon the severity of the bleeding and the size of the baby.

In some cases of intracranial hæmorrhage it is thought that hypoprothrombinæmia may have played some part, but it is important to remember when treating such cases that giving vitamin K alone will not check the hæmorrhage or set right the damage done. Rest, sedatives, hypertonic salines, intravenously or rectally, careful feeding and handling must all be included in the regime of treatment.

(3) *Hæmophilia* is an hereditary disease, transmitted through females to males only. There appears to be absence of an as yet unidentified substance in the blood of these individuals which interferes with the breakdown of platelets to release thrombokinase, when a blood vessel is damaged. The number of platelets is not reduced but the blood coagulation time is markedly delayed, because prothrombin is not active. Usually, affected infants do not bleed following birth or during the first few months of life. Sometimes bleeding after circumcision may be caused by this deficiency. At any time, a trivial cut or bruise may produce intractable bleeding, which is dangerous, not so much because of its quantity, but because of its persistence. Bleeding into and around joints may give rise to a preliminary diagnosis of acute rheumatism. The anæmia produced is hypochromic with a low colour index. There is no abnormality of the white cells and there are no immature cells. There is no specific cure.

Prophylaxis is all important—The bleeding may be stopped by pressure over the affected area with a tampon soaked in a one in ten thousand dilution of viper venom. If this is not available, freshly drawn human blood applied to the wound will

control the oozing by inducing coagulation, but the clot thus formed will be very fragile. Small transfusions may be given before essential operations, when they will act as an effective hæmostatic agent for a few days.

Normal coagulation time is 1 minute 40 seconds up to 2 minutes, by the Dale and Laidlaw method. Normal bleeding time is 4 to 5 minutes.

HÆMOLYTIC CAUSES LEADING TO BLOOD LOSS

(A) *HÆMOLYTIC DISEASE OF THE NEWBORN (ERYTHROBLASTOSIS FŒTALIS)*—About 85 per cent of human beings belong to the Rh-positive blood group. The remaining 15 per cent. of people are called Rh-negative because their red cells do not contain Rh antigen (Boorman *et al.*, 1944). If blood from an Rh-positive donor is introduced into the circulation of an Rh-negative recipient the serum of the latter will probably manufacture Rh antibody which is called anti-Rh agglutinin. This may be produced in the blood of an Rh-negative mother from the child of an Rh-positive father *via* the placenta. The anti-Rh agglutinin then passes back into the blood of the child and reacts with the Rh antigen of the Rh-positive child, causing hæmolysis. Further subgroups of the Rh factor have recently been recognized, such as Rh₁, Rh₂ and rh which may account for delayed reactions and those cases of hæmolysis which occur when both mother and child are Rh-positive. These subgroups may also account for the changes found in the acute hæmolytic anæmia of childhood, described by Lederer, the cause of which has hitherto remained obscure.

Hæmolytic disease of the newborn occurs once in four hundred births, approximately (Javert *et al.*, 1942). In 1941 Levine *et al.* showed that 90 per cent of these cases were due to iso-immunization of an Rh-negative mother by an Rh-positive fœtus. In 1944, Boorman *et al.* demonstrated that 97 per cent. of cases were due to anti-Rh agglutinins in the blood of an Rh-negative mother, whilst 3 per cent were due to atypical anti-Rh agglutinins or more than usually potent anti-A or anti-B agglutinins, which were antagonistic to the red cells of the fœtus. There is usually a family history of several miscarriages or still-births, following a normal first baby. On the other hand, an affected mother may have several living babies, some of whom showed a varying degree of this disorder after birth.

In the infant, three distinct manifestations of this disease may occur. In the fœtus, generalized œdema (hydrops fœtalis) is not consistent with a live birth. In the newborn, the condition may occur with jaundice (icterus gravis neonatorum) or without jaundice (anæmia gravis neonatorum).

Hydrops fœtalis is incompatible with more than a few hours of life, if the baby is born alive at all. There is generalized œdema and the blood count shows a high erythroblast count. The liver and spleen, together with the bone marrow, show overaction at post-mortem examination.

Icterus gravis neonatorum is characterized by jaundice, present at birth or very shortly afterwards, which usually lasts for seven to ten days and then fades, leaving a very pale infant. The stools may be normal or pale. The urine is usually bile-stained. The liver and spleen are enlarged. There is a severe anæmia with a high

proportion of erythroblasts in the film. Later, changes in the central nervous system may arise in those babies who survive, due to the production of kernicterus.

Anæmia gravis neonatorum shows a marked degree of anæmia from a very early age, or its appearance may be delayed for one or two months. There is little jaundice. The spleen is enlarged and there is bilirubin in the urine. The blood shows normoblasts and reticulocytes, and the erythroblast count is always high. The progress of the anæmia is rapid and the baby becomes listless, sucks badly, and is liable to contract infections about the end of the first week. In favourable cases the condition will ameliorate during the third week of life, even without treatment, but this result should never be anticipated.

Treatment depends upon a sure diagnosis. When a mother is known to have had several dead babies it is a wise plan to determine the Rh category as well as to know her blood group. If she is found to be an Rh-negative individual the baby should be grouped immediately and a search made for anti-Rh agglutinins in the mother's blood. If the infant shows suggestive symptoms at birth or thereafter, a definite diagnosis must be made as already described. While the reports are awaited the infant may be given vitamin K or its analogue, naphthoquinone, by injection (0.5 to 1.0 mgm.) As soon as it is established that the baby is suffering from hæmolytic disease, a transfusion of Rh-negative blood, of the same group as the baby, should be given without delay; 10 to 20 c.cm. per pound body weight should be given by the intravenous drip method. This should be repeated after the first twenty-four hours. If this blood cannot be obtained, then Rh-negative blood of group O (group 4 Moss) should be used. If both these types are unobtainable, it is better to use the mother's known Rh-negative blood, rather than to introduce Rh-positive blood into the infant's circulation. Should the mother's blood belong to the Rh-positive category, but there is evidence of anti-Rh agglutinins in her serum, then the blood to be transfused must be compatible with the baby's red cells and with the mother's serum.

The breast milk must be expressed for the first few weeks and boiled before giving it to the child, as it has been demonstrated that the anti-Rh agglutinins are excreted through the breast (Witebsky and Heide, 1943).

Lederer's acute hæmolytic anæmia—It is now thought that the cause of this syndrome is a hæmolytic state produced by incompatibility between the serum of the mother and the red cells of her child, both of whom are Rh-positive but the Rh antigen belongs to one of the subgroups of Rh, together with some other obscure precipitating cause. This latter supposition must be accepted in order to explain the delayed action of the hæmolytic process. The symptoms may begin abruptly in infancy or later childhood with an attack of jaundice, accompanied by fever and perhaps hæmaturia. Extreme lassitude supervenes and the spleen and liver usually enlarge rapidly. Early diarrhœa, vomiting, sore throat and epistaxis often obscure the early diagnosis. The blood shows a marked anæmia with a red cell count of only one million at the first blood examination, the fragility of these cells usually being normal. There is an increase of the reticulocytes but few, if any, megaloblasts. There is usually a leucocytosis, with an increase of myelocytes, but a leucopenia is sometimes found.

If untreated, the tendency is for the anæmia to become permanent.

granulocytopenia and thrombocytopenia. Early transfusion with the appropriate blood group quickly improves the symptoms. Further transfusions and vigorous iron medication may be needed to restore the destroyed blood to normal.

(B) *CONGENITAL HÆMOLYTIC JAUNDICE OR ACHOLURIC FAMILIAL JAUNDICE*—This condition rarely attracts attention during the neonatal period. Most commonly it begins later in childhood, the jaundice following some physiological stress, such as fatigue or infection. It is a rare, familial disease, with recurrent bouts of jaundice of varying intensity. This jaundice is the result of crises of hæmolysis of the red cells, during which they are seen to be of an abnormal shape and size. The red cells are unduly fragile, abnormal in shape (spheroids) and size (microspheroids). Their increased fragility, in saline solution, is characteristic although the severity of each attack cannot be assessed by this sign alone. The spleen is enlarged, as a result of its activity in breaking down the abnormal cells. The urine is free from bilirubin and the stools are normal in colour.

The first attack is usually thought to be one of infective jaundice, unless the patient belongs to a recognized family in which the hæmolytic tendency is dominant in the Mendelian manner. Crises may occur as often as every three months, with fever, prostration and pallor preceding the jaundice. The spleen and liver are enlarged and tender and anæmia develops rapidly. Rarely, such a crisis is fatal. More often the condition begins to improve in three weeks. As the child grows older there is a tendency to decreased severity and number of attacks. The blood findings are characteristic of the hæmolytic nature of the disease, with evidence of attempts on the part of the bone marrow to bring about blood regeneration. The red cells are reduced to about 1 million per c mm, are unusual in shape and size and are more nearly spheroidal than normal red cells. It is thought that this shape makes them more vulnerable during the crisis and contributes to their intravascular breakdown, with the consequent jaundice. Nucleated red cells, usually normoblasts, are frequently found, and reticulated cells, together with variation in the staining property of the red cells, are usual. Bleeding and coagulation times are normal.

Treatment consists in splenectomy, undertaken between the crises, if these are frequent and severe. Results are poor if this is done during a crisis. Alternatively some authorities recommend ligation of the splenic artery or X-ray treatment of the splenic area. If blood transfusion is necessary it should be done after splenectomy so that the hæmolysing organ is no longer active. If surgery is not undertaken, the anæmia must be corrected by giving a good diet, high in first-class protein, with increased vitamins and added iron. Avoidance of infection should be stressed.

(C) *SICKLE CELL ANÆMIA* occurs only amongst persons with African heritage. It is a rare hæmolytic anæmia, caused, or exaggerated, by the typical shape of the red cells and their abnormal structure. The red cells are considerably reduced in number but the hæmoglobin is not severely affected. Leucocytosis is always present. Treatment with 100 per cent. oxygen inhalation without interruption for several days is said to improve the hæmolysis.

(D) *COOLEY'S ERYTHROBLASTIC ANÆMIA OR MEDITERRANEAN TARGET-CELLED ANÆMIA*—This anæmia is endemic among certain families in the Mediterranean area. The fundamental defect appears to lie in the unusually thin nature of the red cells. The combination of jaundice, a varying degree of

æmia, skeletal changes as shown by X-ray pictures and the typical thickening of the face and skull bones, together with the morphological changes in the red cells, make up the characteristic picture of the disorder. There is marked splenomegaly, and moderate increase in the size of the liver. The blood shows a variable æmia, the red cells sometimes being as low as one-and-a-half million, with a high normoblast count but no megaloblasts.

The treatment advised is splenectomy, together with a good diet and added vitamins and iron to correct the anæmia.

(E) *POISONS EXERTING LYTIC ACTION ON THE RED CELLS*—During childhood, any of the following toxic causes may produce a hæmolytic effect on the red cells. Congenital syphilis or the arsenicals used to treat this may have a hæmolytic action in certain individuals. The parasites of malaria or merozoites set up a hæmolytic action, which must be dealt with energetically after the parasites have been destroyed. Blackwater fever, although rare in children, is probably due to this occasional hæmolytic action. Hypersensitivity to any of the sulphonamides may result in a breakdown of the red cells as well as of the leucocytes. Bacterial infections, especially those due to the hæmolytic streptococci, notably in septicæmia, bacterial endocarditis and osteomyelitis, may produce a further load for the patient to bear, in the removal of the red cells by hæmolysis.

VON JAKSCH'S SYNDROME

This is not a disease entity but a collection of symptoms associated with a variety of irritations and stimulations of the bone marrow. Many different causes acting on the red marrow may produce an identical blood picture. von Jaksch originally described a chronic anæmia with a marked leucocytosis, accompanied by moderate splenomegaly and possessing a fairly good prognosis. The anæmia is severe, of a low colour index, with normoblasts, erythroblasts and megaloblasts constantly in the film. The leucocytosis is always high, sometimes as high as 70,000 per c mm, the cells are mainly lymphocytes. Since infection plays a part in the etiology, neutrophil granulocytes are also increased. In addition to the splenomegaly there are hepatomegaly and widespread lymph-gland enlargement.

The syndrome is found accompanying rickets, congenital syphilis and other chronic infective processes and in malnutrition, especially when there is gross iron deficiency in the diet. Three etiological factors are thus known, iron deficiency, hæmolysis and marrow damage.

Treatment depends upon removing the iron deficiency by large doses of iron while the complicating infections are being dealt with. The results of the marrow damage must be remedied by blood transfusions of the appropriate group.

References

- Allibone, E. C., and Baar, H. S. (1943) *Arch Dis Child*, 18, 146.
 Baar, H. S. (1941) *Lancet*, 2, 775.
 Boorman, K. E., Dodd, B. E., and Mollison, P. L. (1944) *J Obstet Gynec*, 51, 1.
 Brokaw, K. F., Sedam, M. S., and Cassirer, A. M. (1942) *J Pediat*, 21, 769.
 Dameshek, W. (1945) *New Eng J Med*, 232, 250.
 Davidson, L. S. P., et al (1943) *Brit med J*, 2, 95.
 Javert, C. T., et al (1942) *Surg Gynec Obstet*, 74, 1.
 Levine, P., et al (1941) *Amer J Obstet Gynec*, 42, 935.
 Mackay, H. M. M. (1933) *Arch Dis Child*, 8, 251.
 —, Dobbs, R. H., and Bingham, K. (1945) *Ibid*, 20, 56.
 Witelski, E., and Heide, A. (1943) *Proc Soc exp Biol Med*, 52, 280.

and non-thrombocytopenic types. It is usually customary to divide each of these two great classes into primary and symptomatic groups, the latter being those in which purpura occurs in the course of some recognizable infection or other form of poisoning. Purpura, as a symptom of the action of some recognizable nova, may in many cases occur with or without a lowering of the platelets in the circulating blood, and the attempt to define thrombocytopenic and non-thrombocytopenic groups of symptomatic purpura inevitably leads to much overlapping and confusion. For clinical purposes the matter of supreme importance is the recognition of the essential thrombocytopenic purpura (Werlhof's disease). Once this is recognized the other purpuras fall readily into their place.

ESSENTIAL THROMBOCYTOPENIC PURPURA WERLHOF'S DISEASE

This condition is invariably associated with a gross diminution in the number of platelets in the circulating blood. For reasons which will presently appear it is certain that this diminution of the platelets is not the cause of the purpuric manifestations, but it is invariably present, and the diagnosis cannot be regarded as confirmed until it has been demonstrated.

The blood platelet count—In normal blood, platelets are usually present to the number of between two and three hundred thousand per c mm. It is usually stated that hæmorrhage is likely to occur when they fall below 60,000 per c mm, they may fall much lower than this without the appearance of purpura, and it would be more accurate to say that the red cells in this condition do not escape beyond the capillaries so long as the platelets remain above this figure. The counting of platelets is a somewhat tricky business and estimates are likely to vary with the technique used and with the observer, for practical purposes the examination of a simple stained film of the blood gives a good idea whether or not a condition of *thrombocytopenia exists*. In films of the normal blood, platelets occur either singly or in small clumps scattered freely among the red cells, in thrombocytopenia the almost complete absence of platelets is immediately striking, many fields will show none at all, and when seen they will be occurring singly and will probably be larger than normal. The examination of a stained film of the blood is an essential step in the diagnosis of thrombocytopenic purpura, not only for the demonstration of thrombocytopenia, but also for the exclusion of other conditions, such as the leukæmias, which may give rise to symptomatic purpura, either with or without deficiency of the platelets.

Clinical signs—Thrombocytopenic purpura is essentially a disease of children and young adults. It rarely makes its appearance after the age of forty. Except for such as may be due to persistent bleeding from mucous surfaces, with the resultant anæmia when this bleeding is prolonged and profuse, it is usually associated with little or no malaise. The onset of the purpuric manifestations may be sudden and dramatic, but more usually there is a prodromal period during which there is susceptibility to bruising on slight trauma, sometimes there may be epistaxis. Examination of the blood at this time will show the characteristic thrombocytopenia. The latent tendency of the capillaries to allow escape of the red cells may become overt as the result of an infection, such as a sore throat, or it may occur spontaneously without apparent cause.

When the latent capillary weakness does become clinically significant it may do so with every gradation of severity. The sole manifestation may be a few scattered petechiæ on the skin surface, at the other end of the scale cases may be met in which the appearance of widespread and gross purpura is associated with hæmorrhage from any or all of the mucous surfaces, so prolonged and intractable as to endanger life. In females, the condition may first show itself at the onset of the menstrual flow. In such cases the first uterine bleeding may be prolonged over many days and extend from one period right through until the next. Symptoms have been known to make their first appearance in young females during pregnancy, with catastrophic results.

TREATMENT—*Removal of the spleen* in this condition puts an immediate and dramatic stop to all purpuric and hæmorrhagic manifestations. They may return later but never in so severe a form as before splenectomy. Why removal of the spleen should have this effect is not understood, it is true that removal is followed by a rise in the circulating platelets, but this rise takes place over a number of days, whereas the cessation of hæmorrhage is immediate on the cutting off of the spleen from the circulation. It seems that some hormonal or humoral mechanism is at work here, and there is some evidence that this involves, not only the spleen, but with it the suprarenal cortex and the anterior lobe of the pituitary body.

In cases of thrombocytopenic purpura in which bleeding from mucous surfaces is so prolonged and profuse as to endanger life, splenectomy may have to be undertaken as an urgent measure. Such cases may be met with in young females with profuse uterine hæmorrhage. Undertaken as an urgent operation, splenectomy carries a fairly high risk, and in all cases of severe hæmorrhage a trial should first be given to blood transfusion. For this purpose it is essential that the infused blood should be freshly drawn, certainly not more than three days old and the fresher the better. Blood stored for longer periods, although valuable in replacing lost red cells, lacks the active hæmostatic power of fresh blood.

Fortunately, in the great majority of cases thrombocytopenic purpura manifests itself as a relatively subacute or chronic state associated with periodical bouts of petechial rash and occasional mild bleedings from mucous surfaces, with intervals of relative quiescence. Such cases should always be observed for a time before splenectomy is seriously contemplated. In a good many instances the capillary dysfunction disappears in course of time. If, however, the manifestations persist, and always granted that the diagnosis has been firmly established, splenectomy should be performed during a quiescent interval. This is particularly important in women in whom the exacerbation of symptoms during a pregnancy may give rise to grave risk of losing both mother and child. Fortunately, in females the menses give good evidence as to whether or not the purpuric and hæmorrhagic tendency is persisting. So troublesome is the uterine bleeding in many cases that it alone necessitates the taking of active steps.

The mere demonstration of a diminution of the platelets does not constitute a diagnosis of essential thrombocytopenic purpura, and it cannot be too strongly insisted that it is only in the essential type that splenectomy is of benefit. Certain of the symptomatic purpuras which will be discussed later may give rise to purpura associated with a diminution of the platelets, the diagnosis of essential thrombo-

vitamin K in the synthesis of prothrombin and no benefit will result. In obstructive jaundice without severe liver damage, however, vitamin K will rapidly restore the blood to normal coagulability with disappearance of the purpuric and hæmorrhagic tendencies.

Purpura is an important part of the clinical picture of *scurvy*. It has been widely accepted that scurvy is due solely to a deficiency of vitamin C or ascorbic acid; there is some evidence that although the asthenia and constitutional symptoms of scurvy are due to deficiency of ascorbic acid the actual purpuric manifestations may be due in large part to deficiency of vitamin P. This is available as a synthetic preparation and may be combined with ascorbic acid in the treatment of scurvy, but it is safer to make use of natural sources, such as fresh fruit and vegetables or germinating grain, known to contain all the antiscorbutic factors, among which there may be others, as well as the recognized vitamins C and P.

Reactions of sensitive persons to certain drugs may be associated with purpura, these should probably be properly regarded as anaphylactoid phenomena and not as due to any specific action on the part of the drug. The most important examples are *iodides*, *bismuth*, and *salicylic acid*.

Finally, purpura may occur as the result of weakening of the capillary walls in *old age*. This senile type of purpura is usually confined to the legs, it is of no particular clinical significance and only calls for investigation of the patient's diet to make sure that there is not also an element of vitamin C deficiency.

CONCLUSION

Purpura must always be regarded as the manifestation of an underlying morbid process.

In *symptomatic purpura* the purpuric manifestations are not in themselves of great importance and, except in the case of the vitamin K deficiency associated with obstructive jaundice, do not call for any particular treatment.

Anaphylactoid non-thrombocytopenic purpura likewise, although it may be the most striking manifestation of the morbid process, does not itself call for treatment.

The case of *essential thrombocytopenic purpura* is entirely different. In this condition the purpuric and hæmorrhagic manifestations constitute the outstanding feature of the disorder and may themselves endanger life. The disturbance centres upon the spleen and can be brought to a cessation or profoundly mitigated by its removal. On this account recognition of essential thrombocytopenic purpura constitutes a main factor in the differential diagnosis of the purpuras, and the exclusion or establishment of this diagnosis is of the utmost importance in the investigation of any case of purpura.

GLANDULAR FEVER (INFECTIOUS MONONUCLEOSIS)

By SIR HENRY TIDY, K.B.E., M.D., F.R.C.P.

Consulting Physician, St Thomas's Hospital

GLANDULAR fever or infectious mononucleosis may be defined as an acute infectious disease characterized by enlargement of the lymphatic glands, changes in the blood cells, especially mononucleosis, and a uniformly favourable course. This definition gives no hint of the protean forms in which it appears, and new manifestations are still being recognized.

Three periods can be recognized in the history of glandular fever —

(1) *Clinical period* (1889-1920) —The disease was first described by E. Pfeiffer in 1889. It struggled for existence until about the year 1900, by which date it was considered to be completely discredited and there is little literature on the subject in the next twenty years.

(2) *Hematological period* (1920-1932) —In 1920-21 the development of mononucleosis in the blood was described by Sprunt and Evans (1920) as infectious mononucleosis and by Tidy and Morley (1921) as a feature of glandular fever. The disease was thus resuscitated, and with this guide the clinical manifestations were more clearly studied. It must be noted that Burns in 1909 fully described the lymphocytosis in a series of cases diagnosed as glandular fever, but this article was entirely overlooked until Bernstein's review in 1940.

(3) *Agglutination period* —This period dates from the discovery by Paul and Bunnell in 1932 of heterophil agglutinins in the blood.

CLINICAL GROUPS

During the years after 1920, when the clinical features were being carefully studied, it became customary to separate several clinical types. Whilst many cases fall easily into such groups, every intermediate form and combination of types may occur. With increasing knowledge such groups may be abandoned, just as the numerous Victorian types of typhoid are now obsolete. They will be briefly mentioned —

(1) *Glandular fever in children* —This is the form in which glandular fever was first recognized. It is especially common in England, in resident "preparatory" schools, between the ages of eight and fourteen years. The cervical glands enlarge rapidly and form a definite mass, the most characteristic feature being the presence of glands deep to the middle of the sterno-mastoid muscle. Glands elsewhere may also enlarge. Rashes are rare.

The temperature may be high for a few days, but constitutional symptoms are not severe and the illness does not as a rule last for more than two to three weeks, by which time the mass of the glands has subsided. Suppuration is practically unknown. Mononucleosis is often, but not always, recognizable at the first examination, otherwise it develops within a few days of onset. Under the age of five years the picture is less characteristic.

typical blood changes, the glandular enlargement, and the neurological symptom develop, or in their comparative severity. In the case of Epstein and Dameshe (1931), the glands, lymphocytosis in the blood and in the cerebrospinal fluid, and the meningeal symptoms developed and subsided together. Also in a case recorded by Nyfeldt (1938) the mononucleosis in the blood and cerebrospinal fluid fell together. But this is by no means constant. In the case reported by Sucher and Schwarz (1936) the illness fell into two phases, the first exhibiting common glandular and blood changes with but slight meningeal symptoms. These subsided, but after an intermission severe nervous symptoms developed with hemiplegia, convulsions and coma, and monocytosis in the cerebrospinal fluid. The blood at this stage was normal and the glands not enlarged. There was rapid and complete recovery.

In four cases, at least, the initial blood count has been normal or shown a moderate polynucleosis. For example, in the first case of Thelander and Shaw (1941), the cerebrospinal fluid contained 630 mononuclear cells and the blood count was 15,000 leucocytes with 75 per cent polynuclears. Later the blood became typical. Heterophil agglutination was positive. In the case of encephalitis recorded by Landes *et al* (1941) the initial white cell count was 11,000 with polynuclear 50 per cent. The pathologist did a Paul-Bunnell reaction which was positive. Landes states that the diagnosis would not otherwise have been suspected. In both these cases the glands did not enlarge at the onset, becoming palpable on the thirteenth and twenty-second days, respectively.

In the more severe neurological forms the blood changes tend to be late and the glandular enlargement not greatly marked, as with other severe types of glandular fever.

Neurological symptoms may be present without changes in the cerebrospinal fluid, probably due to encephalitis. This occurred in Landes's case and in one of Pietzonka's (1939) cases. Neurological complications probably are not rare. I have seen two cases in the last three years and heard of another, all as yet unpublished. One case had severe oedema of the eyelids, which was also present in a case of Nyfeldt's. The cerebrospinal fluid has been examined as controls in a few cases of glandular fever without neurological symptoms. The results vary. Of Kilham's and Steigman's three cases (1942), two were normal and one showed monocytosis, and two of Nyfeldt's controls also showed monocytosis. In no case has the cerebrospinal fluid given a positive heterophil agglutination.

The diagnosis of glandular fever is clearly liable to be overlooked in the presence of neurological complications. This is especially so in the severer forms in which the glandular enlargement is usually late and slight, and the early blood count shows a moderate polynucleosis or a normal result and is often not repeated.

HETEROPHIL ANTIBODIES

The term heterophil antibodies is applied to antibodies which can react with certain antigens which are unrelated to the cause of their development. Here it is a question of antibodies in human serum which agglutinate sheep's red corpuscles.

Such heterophil antibodies may be present in low titre in normal serum, and similar but independent antibodies may be present to a higher titre in serum

sickness or after injections of horse serum Paul and Bunnell, in 1932, made the curious discovery that heterophil agglutinins develop in high titre in human serum in glandular fever and in no other disease, with some academic exceptions. The three types of agglutinins are not identical and can be separated by appropriate absorption tests. Barrett (1941) made a careful study of this aspect.

The serum agglutination test—The technique has not been standardized. A simple method, such as that clearly described by Smeall (1942) is quite satisfactory for clinical purposes. Bernstein (1940) states that confusion has arisen in America over the method of recording the dilution of serum, but this does not seem to have occurred in this country. The final dilution of serum of course must be taken in recording the titre.

With Smeall's technique, a titre of 1/64 is practically proof of glandular fever and a titre of 1/128 is absolute proof. If there is any doubt when the titre is 1/64 or under, the test can be repeated to observe if there is any variation in the titre, or absorption tests performed.

The titre has no constant relation to the severity of the disease or to the degree of lymphocytosis. The reaction may be positive in the absence of glandular enlargement. Bernstein found a positive reaction in one case before the development of mononucleosis. The reaction has no relation to the transient positive Wassermann reaction which is sometimes found.

Important questions are—how often is the reaction positive in glandular fever and at what stage does it become positive?

It would appear that the reaction becomes positive a short time before the termination of active symptoms. Milder symptoms may continue subsequently for as long as two weeks, but it is striking how often severe constitutional symptoms in the long febrile forms rapidly ameliorate within a few days of the reaction becoming positive. Thus the development of a positive reaction is related rather to the end of the attack than to the onset, and may well be connected with the development of immunity, as Himsworth (1940) has suggested.

In the mild juvenile glandular type often seen in Britain, and in the infectious mononucleosis types of adolescence common in America, the reaction is frequently, although not invariably, positive at the first examination, which is usually four or five days after the onset. If the examination is earlier, the test may be negative or the titre may be suggestive without being diagnostic. The titre may rise further in the next few days. In these types the symptoms and blood changes are often accepted as sufficient to establish the diagnosis and the test when negative is not always repeated. Nevertheless, in these cases and these circumstances the test is positive in nearly 90 per cent. In very young children a negative reaction in the acute stage is not uncommon, but it is unknown how often it becomes positive subsequently, as repeated tests are rarely performed. In the severer febrile forms there may be several weeks of pyrexia and constitutional disturbances before the reaction becomes positive, but it rarely fails to become positive before convalescence sets in.

A positive reaction may become negative, or nearly negative, within two weeks of its recognition but often persists for several weeks, and not uncommonly for four or five months. It has been found positive after a year, but this must be rare.

a case in which the parotid was affected. The diagnosis from sepsis is occasionally difficult and a blood count may not be available at the time, but œdema of the neck only occurs in the anginose type. Most cases in which I have been in doubt have proved to be due to sepsis. The anginose type is frequently mistaken for diphtheria, but in spite of the patient's anxiety, toxicity is conspicuously absent and remains so. Theoretically the "bull neck" of diphtheria might be mistaken for the anginose type.

There is an infective condition which may be termed "epidemic cervical adenitis" which has no connexion with glandular fever. The cervical glands are more diffusely and evenly enlarged, occasionally the axillary and other glands are involved. The glands subside rather slowly and pyrexia and constitutional symptoms may persist for several weeks without presenting grave features. There are no blood changes and heterophil agglutinins are absent. The glands never suppurate, angina does not occur and recovery is complete. There was a considerable number of cases in the Army in 1941-42. The difficulty in diagnosis is mainly from lymphadenoma.

The blood changes should not cause difficulty when the patient is seen during the acute stages of the ordinary forms. In acute leukæmia the constitutional symptoms are always severe and the diagnosis is rarely in doubt.

An important and extremely difficult diagnosis is from the rare, slowly progressive, chronic lymphoid leukæmia. This disease may have periods of pyrexia with moderate increase in the size of the glands and only slight constitutional disturbances. The lymphocytes may then be only at the upper limits of normal or slightly above. The distribution of the glands does not correspond with that characteristically found in glandular fever but the difference is scarcely diagnostic. It is important that neither the glands nor the blood count change rapidly, and heterophil agglutinins are absent. The most reliable guide is that enlarged glands have often been noticed a year or so before the attack, but this is not infallible. The difficulty is especially great when a patient is first seen some months after the pyrexial attack. Either lymphocytosis or some glandular enlargement may persist for several months after glandular fever, but if both features are present for six months the diagnosis must be considered in doubt, unless it has been fully established, as by a positive heterophil agglutination. I have watched three such cases, originally diagnosed doubtfully as glandular fever, gradually develop into fatal lymphoid leukæmia or lymphosarcoma during periods of three to ten years.

In the severer febrile forms of glandular fever there may be no means of establishing the diagnosis for several weeks. Glandular enlargement, lymphocytosis and heterophil agglutinins may all be absent. This may also apply to onset with jaundice.

Most of the cases with neurological manifestations also fall into this prolonged type. The relation of this group to benign lymphocytic chorio-meningitis is of interest. There are no distinguishing neurological features and the changes in the cerebrospinal fluid are identical. In few, if any, cases of benign lymphocytic meningitis in the literature are data recorded which exclude glandular fever. In cases of glandular fever with neurological complications the specific features, viz mononucleosis, heterophil agglutinins and glandular enlargement, tend to develop

late in the course The glandular enlargement is slight and may only be found on special examination. Early blood counts are of little value, although a moderate polymorphonuclear leukocytosis is suggestive The identity of the two conditions can neither be affirmed nor denied, but the possibility exists and requires consideration, which it has not yet received.

PROGNOSIS

The course is uniformly favourable, only an occasional death having been reported The suddenness and rapidity with which severe symptoms often ameliorate almost resemble a crisis This especially applies to the anginous type but also occurs in the prolonged forms Long convalescence is often required even after mild attacks Formerly ascribed to the blood, this debility may really be due to encephalitis

TREATMENT

The normal course and prognosis should be borne in mind when the value of drugs is being assessed. Many drugs have been claimed to abort attacks and one by one have been discarded. I can find no difference between those so treated and those not. Sulphonamides are valueless and their use should be deprecated in a condition in which the blood-forming tissues are in a sensitive state Antipyretics are contraindicated in severe cases as they aggravate the sweating and increase prostration

References

- Barrett, A. M (1941) *J Hyg*, 41, 330
 Bernstein, A. (1940) *Medicine*, 19, 85
 Burns, J E (1909) *Arch int Med*, 4, 118
 Chevallier, P (1928) *Rev Path comp Hyg gen Paris* (editorial)
 Downey, H, and McKinlay, C A. (1923) *Arch int Med*, 32, 82
 Epstein, S H., and Dameshek, W (1931) *New Eng J Med*, 205, 1238
 Glanzmann, E (1930) "Das lymphomatoide Drüsenfieber," Berlin.
 Halcrow, J P A., Owen, L M., and Rodger, N O (1943) *Brit med J*, 2, 443
 Himsforth, H P (1940) *Lancet*, 1, 1082
 Kilham, L., and Steigman, A. J (1942) *Ibid*, 2, 452
 Landes, R., Reich, J P., and Perlow, S (1941) *J Amer med Ass*, 116, 2480
 Longcope, W T (1922) *Amer J med Sci*, 164, 781
 Marun, L (1941) *Lancet*, 2, 480
 Nyfeldt, A (1938) *Acta Oto-laryngol Scand*, 26, 280
 Paul, J R., and Bunnell, W W (1932) *Amer J med Sci*, 183, 90
 Pfeiffer, E (1889) *Jahrb Kinderh*, 29, 257
 Pretzner, H. (1939) *Dtsch Arch klin Med*, 185, 253
 Richardson, J S (1942) *Lancet*, 1, 618
 Saksena, H C (1942) *Ibid*, 2, 267
 Schmidheiny, M. L (1927) *Schweiz med Wschr*, 1, 241
 Smeall, J T (1942) *Edinb med J*, 49, 291
 Sprunt, T P., and Evans, F A. (1920) *Bull Johns Hopk Hosp*, 31, 410
 Stevenson, E M K., and Gorr Brown, T (1943) *Glas med J*, 140, 137
 Sucher, A., and Schwarz, E (1936) *Wien klin Wschr*, 47, 1417
 Thelander, H E., and Shaw, E B (1941) *Amer J Dis Child*, 61, 1131
 Tidy, H L., and Morley, E B (1921) *Brit med J*, 1, 100

So much for growth and body building Let us turn to consider the population as a whole when diet is important for the maintenance of health, well-being, physical fitness, positive health, or whatever it may be called

THE ECONOMIC FACTOR

Investigations of the League of Nations Committee in 1937 led to some striking conclusions They correlated the average diet according to income level with the following results —

- The dietary of 10 per cent. with the lowest income was in all respects inadequate
- In the next (10 per cent) higher income group it was adequate only in total protein and table fat
- In the next 20 per cent. it was just adequate in energy value but was below the standard in calcium.
- In the next 20 per cent. it was more than adequate, but still showed calcium deficiency
- Only in the 10 per cent. top income class did the diet exceed in all essentials the standard food requisites

Clearly the recent war has provided a gigantic experiment For the first time the even distribution of essential foodstuffs brought about by rationing, the introduction of national flour, and the fortification of certain foodstuffs by vitamins or minerals, have benefited a great section of the population who before the war could not buy an adequate diet

Naturally, the comparatively small number whose diet was unrestricted in economic circumstances have had their intake of many of the essential nutrients substantially reduced below the level to which they were accustomed

WAR-TIME DIETARY

It is estimated that the war dietary in this country is adequate both in respect of caloric value and to protein, the reduction in meat being replaced by an increase of vegetable protein in the national loaf Fat has been considerably reduced as with it as a consequence vitamin A The absence of fruits, especially of the citrus varieties, also results in a deficiency in vitamin C These deficiencies have been met by artificial substitutes It is, in fact, maintained that the present arrangements should be continued as part of the permanent peace-time policy, so satisfactory is the war-time state of affairs resulting in the production, not merely of an adequate diet, but of an optimal diet through the provision of the right constituents in the right proportions and the avoidance of overeating But the need is to budget for human nature as it is, not as it ought to be A nation will accept the inevitable and there is nobody more amenable to discipline than the freedom-loving Englishman when he is convinced of the necessity But how many people wish to be healthy for health's sake? Eating and drinking are not a mere matter of nutrition, much of the enjoyment of life is bound up with the conventions and ceremonies of meals We eat not only to satisfy hunger and maintain nutrition but for sheer enjoyment to gratify the palate, to stimulate, and, it may be said, to pass the time! No doubt many overeat, and like to overeat, and, once adjusted to superfluity, resent reduction and restriction The battle of the loaf will be a bitter one Will return!

white flour be demanded despite the pronouncement that any of the valuable constituents—iron, vitamin B, and protein—are thereby removed? Such deficiencies can be made good by eggs and bacon, an attractive but expensive opportunity which is not available to the poorer classes who have almost an addiction for white flour in any shape or form. Perhaps some day a General Election will be fought on this issue with the competing slogans "Eat the standard national wheat-meal for health" and "In a free country, one should eat what one likes." It might be represented that since laws exist to prevent people from eating and drinking what they like when it is necessary to protect them from the recognizable dangers of poisoning and infection, laws might similarly be enforced against the consumption of flour seriously deteriorated by removal of essential nutriment. The difficulty resides in the contrast of consequences. Nobody can fail to be convinced of the suffering resulting from water-borne epidemics, in regard to the continuance of malnutrition, no dramatic results ensue but an insidious lowering of the general health. And malnutrition is probably a greater danger than under-nutrition. It is necessary, perhaps, to think more in terms of optimal rather than of adequate nutrition. Health is only too frequently regarded as mere absence of disease; the aim should be to think of vitality, of positive, or buoyant, or better than average health. To secure this, food is not the only essential, but it is the most important one. Doubtless the supply of food to the poorer classes one hundred years ago was lamentably deficient. But what they had was good—there was nothing preserved, condensed, frozen, concentrated, synthetic. When it is realized that the symptoms of early scurvy are said to be headache, dizziness, lassitude, gloom, irritability and proneness to condemnatory and uncalled for argumentativeness, it is tempting to explain cases of "war weariness" in terms of subclinical scurvy, considering the scarcity of fresh fruits and other foodstuffs rich in vitamin C.

DIET AND ATHLETICS

It is natural of course in the consideration of physique to think as much of strength as of health. It is popularly supposed that the size and power of muscle, the capacity of heart and lung, energy, stamina and endurance, all of these are to be obtained by the appropriate selection of certain articles of diet. There is something in this, something but not much. It is known that a sufficiency of body-building and energy-creating material must be available when great output of muscular work is demanded, but there is no support for the silly recommendations in some books on athletic training that certain articles of food confer speed, others staying power, others again, strength. These qualities are to a considerable extent natural possessions, they may be developed or improved by training but, so far as foodstuffs are concerned, there is no opportunity for specific influences.

This drastic debunking of certain traditions will not be popular; it leaves no room for the attractively mysterious. How has it come about that so much importance is attached to the subject of diet in athletic training?

In the days when pugilism, pedestrianship and oarsmanship were practised only by professionals, restriction of their customary habits of gluttony and intemperance was the most salutary rule that could be framed and enforced in preparation for

their contests When these feats became fashionable, the amateur naturally imitated these practices of the professionals, more especially since in matters of self-indulgence comparison at that time would hardly have been in favour of the gentleman But, although the original necessity has largely or completely disappeared, the idea has persisted, so that all sorts of traditional restrictions, prohibitions and inconveniences are still accepted Certain articles of diet are credited with athletic virtues, in other articles, evils lurk This or that foodstuff is supposed to be good, this or that bad for the wind, as if respiratory power could by such means be directly influenced In a desire to avoid the wrong path, the early trainers wandered from the right Having learnt that overcooking hardened the fibres of meat and lessened its nutritive power they went to the opposite extreme and ate it nearly raw, swallowing it with as much repugnance as taking physic bolting it in lumps with the aid of the ruggardly allotted liquid, for liquid of all kinds was supposed to be weakening Even in my day the idea was still prevalent that training for a boat race consisted in stuffing as much beef and mutton as possible and then going on to the river and working it into oneself This was precisely reversing the order in which the natural requirement of the body for food should be applied It was trying to perform the conjuror's trick of putting a quart of liquid into a pint bottle without having taken the conjuror's precaution of providing a secret receptacle for the superfluity

Misconceptions relating to the dietetic influence upon athleticism fall into three categories —

- (1) The raw meat regime with elimination of nearly every other form of foodstuff of palatable quality Training in those days was an ordeal from which the strongest recoiled with a shudder There still are people who measure wholesomeness of food by its nastiness!
- (2) Over-alimentation, the idea that food may be pushed into the body as into an empty sack—the more the better The elementary principles of digestion and absorption came in for no consideration whatsoever
- (3) The modern vogue of the food cranks with pseudo-scientific explanation of the virtues of fantastic dietaries, the apotheosis of the vitamins

I have briefly dismissed the first two of these, and, in respect to the third, it is pertinent to say that any great athlete's methods and habits will be closely scrutinized by ambitious admirers who suppose that an imitation of his method is likely to lead to reproduction of his capability and success If he indulges in some particularly queer or unusual practice, so much the better In all probability any such peculiarity, however appropriate to his individual requirement, has no more influence upon his athletic capacity than, say, the circumstance of whether the petrol or oil used for a magnificently tuned-up engine comes out of a green or a red can! The more I have studied and investigated great athletes the more I have become convinced of the trivial effect of diet upon their capabilities The majority eat and drink what they fancy, and because they happen to be Nature's aristocrats they not infrequently exhibit a comparative indifference to accepted laws of hygiene I remember a campaign some years ago to establish the advantage of total abstinence by quoting examples of athletes who never took alcohol This was at once countered by the presentation of examples of equally great or greater

athletes who enjoyed their glass of beer I am reminded of the observation of the great Harry Vardon —“Moderation is excellent in all things, but never have I been beaten by a teetotaller!” One interesting confirmation of my impression of the practice of eating as distinguished from nutritional demand was afforded by my experience of long-distance racing cyclists. I had expected to find a correlation between their enormous physical output and their food intake. But not a bit of it. Their ingestion was in the circumstances surprisingly low. Is this evidence of superior assimilation, that they could extract more from their nutriment than the average person? The physiologists would have none of this. The reason, as I see it, is that the long-distance cyclist is of phlegmatic temperament, he has to be, to endure such monotony and to be indifferent to protracted discomfort and fatigue, and he has the nervous system which is relatively independent of the stimulation which the average person requires through food or, perhaps I should say, eating, and, I may add, also independent of tobacco and alcohol. That he is often a non-smoker and an exceedingly modest drinker are abstinences dictated not in the interests of physical fitness but just because these anodynes do not appeal to him.

FOOD CULTS

Vegetarianism is often advanced as advantageous to the cult of physical fitness as well as of health in general. But it is well to be quite clear about the principle.

We hear from time to time of modern Nebuchadnezzars, and not only as inmates of mental hospitals, who demonstrate what we already knew, the remarkable capacity of the human body to withstand ordeals and insults. For satisfactory existence, vegetarianism in the true sense is surely inadmissible, for the structure of the human alimentary canal makes it absolutely impossible to ingest sufficient nourishment, let alone manipulate the huge bulk of residue that would be unavoidable. In practice, vegetarianism amounts only to abstinence from flesh foods, and on æsthetic and humanitarian lines the principle may well be defended, but this does not come into present considerations. Consider the daily dietary of a vegetarian long-distance cyclist—in ordinary, not war, time of course —

1 lb brown bread
6 oz butter
4 oz cheese
2—3 eggs
1½ pints milk
6 oz oatmeal with brown sugar
Apples, grapes, oranges, *ad lib*

Clearly the caloric value and the provision of all the essentials of a well-balanced diet are guaranteed and it must be a matter of opinion, and by no means easy to prove or disprove, whether there is nevertheless some special advantage in the proteins or other constituents of meat which are not available in the proteins of other foodstuffs, however high their quality. On the whole I think there is, the large majority are better off with flesh foods, apart from the gustatory attraction.

The numerous cults claiming health and strength, such as this, that or the “system”, the ingestion of unfired foods, the advocates of one meal a day

the apostles of complete starvation, may be merely noted and dismissed. All of these may be of temporary advantage to the grossly over-indulgent, but as applied to mankind in general the observations on an individual are valueless. The stimulating effect of an experiment always leads to the sensation of well-being, especially through the feeling of superiority which results from being different from the majority. The subject attributes it to the character of his regime, the dietitian knows otherwise—that pure suggestion is responsible. The effect is psychological, not physiological. Moreover, the adaptability of the human organism must be recognized. Almost any change of dietary, if gradually introduced, can be tolerated. Fresh habits and conditioned reflexes will be established. Once again the fallacy of individual experiment has to be remembered. Only extensive long-term investigations could lead to conclusions that would apply to a nation as a whole.

THE VITAMINS

In the last fifteen or twenty years the vitamins have come into the forefront of popularity. Discovery of their essential importance has led to the belief that on the principle that it is impossible to have too much of a good thing so their introduction on a large scale must result in physical, and even mental, superiority. Naturally the opportunity has been forthcoming of profitable advertising of food-stuffs with large vitamin content and of manufactured products to be taken *ad lib* in tablet form. The best presentation of the position of vitamins was that of Sir Gowland Hopkins who did so much originally to isolate these essentials. He compared them to the nails and screws which, although no actual part of the material, are indispensable in construction and stability. But no rational person would suppose that apart from this function it is necessary to hammer in additional nails! Furthermore, it would be at once admitted that a superfluity would be disadvantageous. So it is with vitamins. Haphazard ingestion is not merely of no advantage but may be a detriment. It is practically impossible to avoid the ensurance of an adequate, and even an optimal, intake of vitamins on any ordinary sensible diet, and only on queer, freak diets is the adequate provision jeopardized. Naturally in times of strict rationing, like the present, more anxiety may be felt. But there is little, if any, evidence that any advantage accrues from a deliberate attempt to increase this, that or the other vitamin beyond their administration through a normal dietary as provided by natural instincts and the customs of generations. Moreover, the superiority of natural products over manufactured ones should be considered. I have the impression that certain valuable, even essential, constituents occur in Nature which have so far eluded analysis and identification.

OTHER FACTORS AND DIET

Other subjects legitimately comprehended under the study of physique deserve at least a passing reference.

There is the ever elusive *obesity* which the physiologists assure us is a simple matter of intake and output. If, they say, a man limits himself to food of an energy

value below his requirements, then, provided he does not develop starvation edema, he is bound to lose weight, unless he has found some method of violating the law of the conservation of energy. That sounds conclusive enough but I feel sure it is not the whole truth. There must be other factors not yet identified. Some, regarded with comprehensible envy, seem to be able to eat and drink everything fancied without stint or discrimination and yet, on account of a self-regulating mechanism, hardly vary a pound over a period of years. Others, who regard themselves as under a sort of curse, are so devoid of flexibility that every scrap taken beyond a rigid restriction is stored up. And even half an ounce a day amounts to nearly a stone in the course of a year. To say that such unfortunates have a familial tendency to obesity is merely a form of words and other equally flatulent explanations are presented to the victims of obesity who have to learn that the only treatment is partial starvation, the elimination of practically everything worth eating.

Then there is *appetite*, which again is by no means the simple matter it superficially appears to be. To say that it is the big feeders who have a good appetite is not at all the same thing as to say that those who have good appetites are the big eaters. The French have a proverb which embodies the difference—"l'appétit vient en mangeant", and, silly as it sounds at first blush, in order to create an appetite it is necessary to persuade the subject to eat, as the scientist puts it, to establish a conditioned reflex or, in more homely phraseology, to run the alimentary canal on a higher gear, to learn the habit of eating, to teach the stomach to expect food. For it is one thing to need nourishment and another to wish to eat.

Finally—*idiosyncrasies*—to say that "one man's meat is another man's poison" is often quite literally true. There is hardly a foodstuff, even the simplest, the slightest trace of which may not produce serious illness in somebody—an "allergic reaction", to use the modern fashionable term. How such idiosyncrasies arise is often plausibly explained, but in many instances they appear to be inborn. Sometimes fanciful prejudices may be overcome by persuasion, but a brutal refusal to recognize genuine natural peculiarities may lead to the infliction of cruel injury to the digestive organs and to the nervous system. Apart from these examples of susceptibility, individuals differ in respect to specific requirements. Some have a craving for sugar, some require large quantities of salt, an outstanding partiality for a particular article of diet may be the exponent of a desire for some ingredient which that article contains, although outside the knowledge of the eater. Different engines work on different fuels and, although observations over a large number of people permit a good working average to be defined, it is well to realize that there is on occasion remarkable divergencies from the average.

THE PSYCHOSOMATIC APPROACH IN GYNÆCOLOGICAL PRACTICE

By ELIZABETH BRYSON, M D

*Physician to the Unit for the treatment of Psychoneuroses, Gartloch
E M S Hospital, Glasgow*

THIS survey is based on the original notes taken by me at the time of consultation, and covers four thousand consecutive cases seen in private practice during the eight years immediately preceding the war. The practice was gynæcological in the widest sense, i.e., that all the patients were women, and the survey will attempt to show as accurately as possible (1) just what are the conditions for which women seek medical advice, (2) how many of these conditions are, or appear to be, without structural basis to account for the symptoms, these being due to disturbance of function related to emotional or psychic stress, and (3) how many seem to be complex conditions in which physical disability and psychic stress are inseparably interwoven.

CONDITIONS FOR WHICH WOMEN SEEK MEDICAL ADVICE

Classification was far from easy and had to be first of all in terms of symptoms, but labels are never wholly true and are always misleading in making that appear simple which is really very complicated.

(A) There were 2,320 patients with gynæcological complaints, and these were grouped under eight headings —

- (1) *Pregnancy group* — There were 513 patients, of whom 108 were unmarried. Some were pregnant; some thought, some hoped, some feared, they were. There were cases of excessive and unnatural fear of pregnancy amounting sometimes to obsession, some cases of the will to abort at any cost; and many cases of anxiety associated with the practice of "coitus interruptus."
- (2) *Menstrual disorders group* — There were 468 cases, of which 212 were menopausal, 87 menorrhagia, 62 dysmenorrhœa, 54 amenorrhœa, and 53 irregular menstruation.
- (3) *Vulvo-vaginal group* — There were 412 cases, comprising 218 cases of vaginal discharge, some gonococcal, some due to *trichomonas vaginalis*, some senile, some due to foreign bodies or neglected pessaries, and some non-inflammatory, 130 cases of pruritus and other conditions of local irritation (twelve showing sugar in the urine), and 63 other vulvo-vaginal conditions, injuries real and fancied, malformations real or fancied, and one malignant case.
- (4) *Pelvic discomfort group* — There were 341 cases, of which 186 were in the child-bearing age-group of under forty-five, and of these, 120 attributed their discomfort to child-bearing; some had been operated upon but still had discomfort. The 155 older women showed the usual variety of cystocele, rectocele and prolapse. There were 67 women requiring

operation, 27 for tumour formation (sixteen fibroids, nine large ovarian cysts, and two carcinomas), and forty in need of pelvic repair

- (5) *Sterility group*—There were 180 women who came for advice because they were not achieving pregnancy when this was desired, and they are included here irrespective of the number of years since marriage or the giving up of contraceptive usage
- (6) *Urinary group*—There were 174 cases, including thirty cases of pyelitis, twenty-four of gonococcal infection, six of glycosuria and eight of albuminuria, many cases of bladder frequency, and some baffling and persistent cases of enuresis
- (7) *Marital group*—There were 142 women who came for advice and examination in connexion with marriage, some normal, some suffering from dyspareunia, and some asking for contraceptive advice.
- (8) *Overweight group*—There were ninety women who came to get help in their efforts to reduce weight.

(B) There was a large group of cases (885) in which "nervous" symptoms predominated so noticeably that they were classed as such, these are detailed later

(C) The remaining 795 cases were not noticeably "nervous" and they did not fit in to any of the well-defined gynæcological groups, so they are classified here "miscellaneous" The cases consisted for the most part of the commoner minor medical conditions and the more casual patients who are seen once only in any medical practice. There were amongst them, however, many complex conditions which will be detailed later

The following table shows this classification—

(A) GYNÆCOLOGICAL CASES	2320
Pregnancy 513 menstrual 468 (menopausal 212)	
Vulvo-vaginal 412 pelvic discomfort 341	
Sterility 180 urinary 174 marital 142	
Overweight 90	
(B) "NERVOUS" CASES	885
(C) MISCELLANEOUS CASES	795
	<hr/>
	4000

CONDITIONS WHICH APPEAR TO BE FUNCTIONAL

The 885 cases noted under (B) as "nervous" had one common characteristic—that no structural basis was found that would account for the many and incongruous symptoms complained of. Physical abnormalities found did not seem to bear any causative relation to the symptoms, or they seemed to be inadequate as an explanation of the symptoms. These cases are accordingly regarded as "functional"

Many were apologetic about seeking advice—"I know there's nothing really wrong with me"—"I know it all rests with myself"—"I shouldn't feel like this"—"I should be able to help myself" A common complaint was "tiredness" "I'm tired", said one woman, "and please don't tell me to rest, I'm tired resting" Another distinguished herself by begging for an interview without an appointment—"I won't keep you a minute, doctor, it's only a nervous breakdown"

The classification of these patients presented many difficulties because of the overlapping and multiplicity of symptoms. Particularly difficult were those in whom repeated operations had been successful mainly in altering the location

of expression of the psychic stress. There were forty cases of psychosis—puerperal manic-depressive, schizophrenic reactions, recurrent depression (a few suicidal) and some obsessional conditions. The remaining 1,193 cases, which include some from group A, are classified with approximate accuracy under the general heading of “neurosis and nervous reactions”, mostly anxiety conditions.

Actual complaints, such as tiredness, queer feelings in the head, fears of pregnancy, of sex, of insanity, excitability, irritability, loss of interest in life, pains all over, coccygeal pain, “too delicate to have a baby”, were classed as “neurosis with subjective symptoms”. Others, such as loss of appetite, nausea, mucous colitis, constipation, throbbing in the stomach, were classed as “somatic symptoms—alimentary”. Palpitation, tightness in chest, tachycardia, were “somatic—cardiovascular”, and some, such as blushing, sudden pallor, fainting, giddiness, disturbances of vision, sweating, coldness of skin, were listed as “vasomotor”. There were some cases of hysterical reaction under emotional stress. In addition to these cases, it was found that there were in nearly every gynæcological symptom-group women whose complaints were persistent and distressing, yet in whom physical examination revealed nothing that would account for the symptoms. Anxiety states and obsessional fears in relation to pregnancy; cases of dysmenorrhœa and menopausal “breakdown”, some cases of pruritus and fears of genital abnormality or malformation, a few sterility cases that seemed to be cured spontaneously when confidence was restored, cases of bladder frequency and enuresis, and anxiety conditions connected with marriage and contraception, make up an estimated total from these groups of 348 cases which will be classified as “nervous reactions with somatic symptoms referred to the genito-urinary system”.

CLASSIFICATION OF 1,233 FUNCTIONAL CASES

PSYCHOSIS	40
NEUROSIS and NERVOUS REACTIONS	
<i>With subjective symptoms</i>	
Fears 179 fatigue 114 insomnia 102 depression 71 head-	
ache 52 hysteria 34	552
<i>With somatic symptoms</i>	
Alimentary 146 cardiovascular 83 vasomotor 64	293
Genito-urinary (from gynæcological groups) 348	348
	<hr/>
	1233

CONDITIONS WHICH APPEAR TO BE COMPLEX

There were in every gynæcological symptom-group women suffering from conditions that appeared to be complex, in the sense that the physical and the psychological elements were so interwoven that they could not be separated. Both sides to the complaint had to be recognized and both had to be treated if relief was to be attained. In some instances the physical symptom seemed to be called forth by the psychic need, as in some cases of dyspareunia; in others it appeared as if the psychic need was not so much causing the symptoms as using an already determined physical disability or tendency, this mode of expressing psychic stress being well exemplified in cases of pelvic discomfort persisting on a basis of pelvic damage. In many it was not possible even to guess which was causative, the physical or the psychical. The taking of a careful history, i.e., listening to the

patient, will often relieve a backache, and the relieving of a vaginal irritation will often cure an anxiety

Other examples of the complex condition are some cases of dyspareunia. Many are psychogenic and yet vaginal spasm and an inflamed and irritated vaginal mucosa (made worse by abortive attempts at intercourse) complete a vicious circle that cannot be broken without the restoration of local confidence. But no local treatment will cure unless it carries with it psychological enlightenment and conviction.

The attitude to all these complex cases was an impartial acceptance of the complex condition, and the aim of all investigation was to discover, not whether the trouble was functional or organic, but how much of it was functional and how much organic; and the aim of treatment was to treat the dual condition.

It was estimated that in the 2,320 gynæcological cases already detailed, 1,040 were complex in the sense here indicated.

In the miscellaneous group there were many complex conditions, but as no claim can be made to the same approximate accuracy as was possible in the other groups a safe under-estimate of these conditions will be given. Thus there were many hæmorrhoidal conditions which were not uncomplicated, breast pains, low blood pressures which defied ordinary understanding, functional dyspepsias, cases of thyrotoxicosis, cases of male hair distribution with many and varied psychological accompaniments, the notoriously uncertain cases of fibrositis, anæmia, and skin conditions in great variety—shingles, acne, dermatitis of various kinds, psoriasis, urticaria—and some cases of asthma. To claim that 200 of the 795 cases in this group are "complex" is to err on the safe side. The final estimate is therefore that in 4,000 cases 1,240 were complex.

TABLE TO SHOW INCIDENCE OF FUNCTIONAL AND COMPLEX CONDITIONS IN 4000 CASES

	Functional	Complex	Others	Totals
(A) GYNÆCOLOGICAL	348	1040	932	2320
(B) "NERVOUS"	885			885
(C) MISCELLANEOUS		200	595	795
	<hr/> 1233	<hr/> 1240	<hr/> 1527	<hr/> 4000

The conclusion from this survey is that in a series of 4,000 consecutive cases seen during a given period in a specified private medical practice (with no contract work and no hospital appointment), 1,233 of the patients were estimated to be suffering from functional conditions, and 1,240 from conditions in which both physical and psychical factors were present, so that nearly 2,500 of the 4,000 patients were such as to require, for their understanding and relief, some psychological knowledge on the part of the physician, and on their own part some psychological readjustment.

The cases reviewed presented the greatest possible variety in gynæcological conditions, ranging on the physical side from simple leucorrhœa to fibroid tumours and carcinoma, and on the psychological side from the natural anxiety associated with an illegitimate pregnancy to sex obsessions and depressive psychosis. The number of psychotic cases was forty and the number of women requiring major surgery was sixty-seven, so that it is clear that whilst the extremes requiring

specialist surgical or psychiatric treatment were touched, yet the great bulk of the work falls within the sphere of the practitioner. But it is clear, also, that to deal helpfully with this great bulk of work the practitioner must be specially equipped.

THE PSYCHO-PHYSICAL INTERACTION

It was noticeable that many of the women had not been getting the help they needed. They were anxious to be taken seriously, yet hardly expected to be listened to. Some had been discouraged by previous medical experience and were drifting from one practitioner to another; and some seemed to be sinking through the bog of discouragement into the morass of chronic invalidism.

What are the reasons for this apparent failure of medical treatment? It is difficult to generalize, but from these years of work some clear impressions stand out. One such is that the practitioner must accept responsibility for the patient as a human being requiring help, and that from the moment this responsibility is accepted the work of the practitioner becomes individual and personal work, depending, for its success, upon things that cannot be weighed and measured, such as mutual understanding, confidence, and trust. This human relationship cannot be avoided if the patient is to be helped, because, whether we like it or not, the patient has confidence in a person, *not* in tests, she accepts reassurance from her doctor, *not* from the laboratory reports. The acceptance of the patient at once involves the practitioner in the acceptance of the psychological difficulties that are causing or aggravating her state of dis-ease, and this means listening to her story. Listening may be begun in self-defence, but it quickly becomes an interest, then a habit, then an enlightenment, then a valuable therapeutic weapon. The practitioner has, in other words, accepted the psychosomatic approach to illness.

A second clear impression is that there is a remarkably large number of women who but for this kind of approach and understanding cannot be helped. Yet these women are not in need of specialist treatment and might even be harmed by it. They are wandering, lost, and vaguely unhappy in the shadowy land between the recognized territories of the general practitioner and the specialist. They are in need of the physician who sees the patient as well as the complaint, who is interested in, and sensitive to, the inevitable and ceaseless interaction between the mind and the body, who recognizes at the earliest stages this interplay and can appreciate the many ways in which a physical disability appears to be used to subserve a psychic need, and again, how emotional stress and strain seem to enliven and render insupportable a slight disability, or rouse into harmful activity some organ-predisposed to instability and imperfect functioning.

That the recognition of this physical and psychic interplay is no new thing is sufficiently evident. "He to whom only the outward and physical evil is laid open, knoweth oftentimes but half the evil which he is called upon to cure", wrote Nathaniel Hawthorne, nearly one hundred years ago. Good practitioners have always known this but the old truth needs to be re-emphasized in a "scientific" age, because the object of investigation, the patient, is alive and changeable and full of subtlety. Thus the woman who comes so quietly to the consulting-room is involved, not only in the immediate discomfort that brings her there, but also, and at the same time, in the problem of living—of growing up in the psychological

ence, of adjusting to new physiological demands, of facing new responsibilities and readjusting to old demands. Often it is because her body is hindering or obstructing her in her efforts to make these adjustments that she seeks help but she herself does not know this. She comes, facing the future and carrying a burden that belongs to the past, and she asks to be relieved of a present discomfort. Is it not likely that the present disability is partly determined by past difficulties and failures, and that it owes something also to the uncertainty, the apprehension, the uneasiness, the vague fear, that may so readily lurk in the shadow of the future?

Having accepted the patient in all her complexity the practitioner is in a position to assess her symptoms in relation to her personality. Her present discomfort may then be treated, but, again, constant awareness of the psycho-physical interaction is the price of success. The one aim of all treatment is that the patient may come to "feel better", to feel more "all-in-one-piece", more integrated, more able to face again her normal human responsibilities.

To become psychologically aware, to recognize the psychosomatic nature of many symptoms, to safeguard the patient from the harm of unnecessary surgical procedures on the one hand, and from unnecessary psychiatric treatment on the other, and by adequate understanding and treatment to rescue her also from the dangers of discouragement and the drift into chronic invalidism—this may be a searching and difficult work but it is the true and indispensable work of the family practitioner. The carrying out of this work implies and requires on the part of the practitioner an understanding of psychopathology and a degree of analytical insight as well as a knowledge of physical medicine. But with this approach and his equipment, with sensitive care to avoid trauma, either physical or psychological, and a lively desire to preserve or restore normal physiological functioning, most of the cases met with in practice can be satisfactorily dealt with, and the others, a small minority, can be brought to the care of the specialist in good order and without undue delay.

A third impression that remains is of some revealing phrases that are heard far too often. "Only nerves" is out of date but is still used by the patient to explain the baffling fact that although the "doctor says there is nothing wrong" she still does not feel right. The "negative finding" has something to answer for here. The giving of an opinion carries with it a certain responsibility, and if the opinion is that there is no organic disease this responsibility is increased rather than lessened. The examination upon which the opinion is based should be careful and complete enough to satisfy the patient, who needs, and should have, reassurance and enlightenment as to the cause of her persisting symptoms. It must be borne in mind that diagnosis is not treatment, nor is explanation cure. Easy reassurance without inner enlightenment is not helpful. The patient looks up after the most emphatic and cheerful assertions that all is well and says "but I still feel ill, Doctor."

"Too small" is a tiresome phrase. So many women believe that they are "too small" that one is tempted to wonder how any babies get born at all. Untold harm is done by the use of this phrase to explain early marital difficulties, and nearly always a practitioner is credited with its use. It may be helpful to point out that women are often completely befogged in regard to the anatomy of the

organs, and that in their blind fear they are not adult at all, but are thinking and feeling and re-experiencing in terms of an old childish bewilderment. It is at least possible to avoid adding to their fear, and a good rule is "Never tell a woman that she is too small—not even if it should be true—which it seldom is"

"Of course it's nothing to me" is a surprisingly common remark, and often leads to the unsuspected cause of much "tiredness" Women who thus express their private feelings in regard to marital relations are apparently quite ignorant of the happier possibilities in married life they are not complaining, they regard themselves as normal or perhaps a little superior, and often resent any suggestion that they might be more happily adjusted Frigidity in women, and the use of contraceptives and the attitude towards possible pregnancy, are all closely bound up together, and all closely related to the "nervous" conditions met with in practice. Some women, although not desiring further pregnancy—yet wilt a little in the arid atmosphere of safe contraception—they are not vitally interested

"I've never been the same since" is another revealing remark—"never the same since my baby was born" It is of course pertinent to ask whether a woman should expect to feel the same after the profound experience of carrying and bearing a child It is literally true that she never is, and never can be, "the same" The experience may mean anything, from the abiding satisfaction that compensates for every pain to the hidden resentment that turns every discomfort into torture. But whilst the recognition of this vast variation in individual reaction should keep the practitioner continually aware of the psychic element in every case, there is no need to be blind to the fact that the physical damage and stress vary also—and vary tremendously—in different women The restoration of a woman who has "never felt the same since" may therefore involve anything from a pelvic repair operation to an attempt to alter her unconscious attitude to the whole vital question of pregnancy and child-bearing Many women want a baby and yet resent the loss of physical perfection that child-bearing entails, they have lost the attitude of natural acceptance and have not attained to that of conscious creative surrender As psychological sensitivity in dealing with patients increased, the minor operation became increasingly distrusted and increasingly unnecessary Operating for dyspareunia was discarded and so was dilatation for dysmenorrhœa. Curettage became the rarest of procedures, and advice to have the tubes cut was hardly ever given some women become subtly disintegrated when they realize that conception is no longer possible, and sometimes the husband loses interest in a wife rendered sterile There is a gap between the practising physician and the psychiatrist which must in the interest of the patient be bridged, and it is hard to see how this can be done except by an enlargement of the sphere of the practitioner He has unique advantages—his close contact with the patient, his first-hand knowledge of family peculiarities and tendencies, his appreciation through familiar experience of the humbler difficulties and hesitations and unexpected reserves of the ordinary man and woman But the outstanding advantage is that he alone sees the patient early enough to catch her in the curable stage before the faulty reactions have become fixed and irreversible To do this he must have the requisite interest and knowledge

CHILD HEALTH

XVIII—THE CONTROL OF THE COMMON FEVERS
OF CHILDHOOD

BY C M SMITH, OBE, MD, DPH.

County Medical Officer of Health, Northamptonshire

THE purpose of this article is to discuss some of the administrative and practical points that arise in the control of the common infectious diseases of childhood. Childhood and growing-up, which should be periods of uninterrupted mental and physical development, are too frequently punctuated by attacks of measles, whooping-cough, scarlet fever, diphtheria and the other common infections. Since the fevers of childhood have no biological value whatever, the aim must be to exercise such control that in time they will be completely banished.

Over eighty years ago, Murchison, in his treatise on "Continued Fevers", discussed the relative merits of isolating fever patients or of distributing them in the wards of a general hospital. He quoted a Dr Peacock (1856) as saying that

"when he was a student at Edinburgh, it was determined by the Managers of the Infirmary to try the effect of distributing the patients throughout the other wards in the hope that the poisons might by such means be so diluted as to prove innocuous. As an experiment, four patients labouring under fever were placed in different parts of each ward which usually contained thirty beds and four beds were removed from the ward so that each patient with fever occupied the place of two ordinary patients and their beds were placed in the piers between two windows and these were left constantly open. Notwithstanding these precautions, the fever spread to the patients in the adjoining beds and in a month no less than twelve cases of infection occurred. Nor did the evil stop here, for one patient who had been in a bed next to a fever patient went out, sickened of fever after reaching her home and spread infection in a crowded court in Leith, previously free from any fever."

The fever imported to Leith was typhus!

To return to Murchison, as might be expected, he concludes that the right place for typhus patients is a fever hospital, provided 2,000 cubic feet is allowed to each patient, and that there is thorough ventilation. Whilst typhus, smallpox, and a few of the other major infectious diseases will, so far as can be foreseen, always be isolated in fever hospitals, the pendulum in respect of the isolation of the more common infections is now swinging towards the advantages of isolation at home instead of in hospital.

NOTIFICATION

The local authorities responsible for the control of infectious diseases are the County Borough Councils and the County District Councils, viz, Non-County Borough Councils, and the Urban and Rural District Councils. The object of notification is to enable the local authority responsible for the control of infectious

This article completes the series on Child Health. A new series, entitled "Early Recognition of Disease," will begin in the January, 1946, issue.

to be said for the idea of soaking a sheet in disinfectant and hanging it behind the door. The sheet does not restrict the meanderings of the measles virus or the sojournings of the scarlatinal streptococcus, but it may make prospective visitors think twice about entering the room, and it also serves to remind the mother of the need for strict observance of the ritual advised by the medical attendant.

Most mothers will have many questions to ask and the practitioner could obtain useful and practical help in the home management of a case if, instead of sanitary inspectors being employed to visit cases of notified infectious diseases, nurses whose training included fever hospital work were used to answer all the mother's questions and to show the mother how the practitioner's instructions were to be put into practice, the nurse could also take a spell of nursing at regular intervals to allow the mother a break for fresh air and recreation.

DISINFECTION

Concurrent disinfection has for its object the destruction of the organisms on potentially infective material during the course of the illness. Terminal disinfection describes the measures taken to destroy any infection that may be left in the home after the patient has been sent to hospital or has recovered.

Of the value of disinfection in the control of infectious diseases, Sir William Savage wrote in 1941 as follows —

"At one time disinfection occupied a very important place in the armaments to combat infectious disease since it was thought that much infectious disease was spread through infected inanimate matter (fomites). With the recognition of the carrier case and the enormous importance of spray discharge as a spreading agent, the infected fomites factor has shrunk greatly in importance and significance and now occupies rather a minor place. At the same time disinfection is still of considerable importance when used for the correct purposes."

So far as fever hospital practice is concerned, increasing attention is being given to disinfection in order to control cross-infection. Modern research has shown that respiratory disease can be conveyed, not only by infected droplets from the nose or mouth, but also by droplet nuclei, which are 1 to 5μ in size compared with the former which measure 7 to 100μ . The infected droplet nuclei can remain in the air for a considerable time, and the pollution of the air is greatest after bed-making, sweeping of floors, and so on.

Dust-reducing measures — The new methods in fever hospital practice aim at the reduction of dust by the application to the floors of spindle oil, which traps the dust and prevents it from rising. Bed linen, especially blankets, are a prolific source of infected droplet nuclei after bed-making, and this can be controlled by adding a small quantity of white oil in the final wash in the laundry. The blanket may be said to be a hygienic anachronism, for it cannot stand frequent washing, and it both absorbs dust readily and just as readily yields it up when shaken about in bed-making. The textile research scientists should put their minds to providing an article that will take the place of the blanket as regards its heat-conserving qualities, but which will be as hygienic as a linen sheet.

Disinfection of air — The infected droplet nuclei can also be attacked in the air, either by chemical disinfectants or by ultra-violet rays. The employment of chemical disinfectants such as propylene glycol and triethylene glycol has already been developed to a considerable degree in this country, and it should be noted that

these substances are effective in concentrations as low as one in ten million

Ultra-violet rays have been more used for aerial disinfection in America, where good results in the prevention of cross-infection in schools and nurseries have been reported. In this country, Wright, Cruikshank and Gunn (1944) have reported success in the control of cross-infection by hæmolytic streptococci in measles wards by the use of all the above methods except ultra-violet rays. Whilst the methods here described are at present restricted to comparatively few hospitals, it is by no means unlikely that if the success already reported is confirmed, application of some of these measures will be found useful in the control of infection in cases treated at home, and as housing conditions and domiciliary medical and nursing services improve the proportion of cases treated at home may rise in the future.

Although, as Savage says, disinfection has shrunk in importance, this has been largely due to much of the practice not being based on scientific principles, and on account of the recent research work in dust-reducing methods and aerial disinfectants, it can be said that disinfection is now coming into its own again, occupying a relatively greater position.

The steps to be taken either concurrently or at the end of the illness must depend upon the viability of the organism outside the human host. Savage has a useful division of diseases as follows—

Group A Infectious diseases for which concurrent disinfection is required, but not terminal disinfection—Cerebrospinal fever, influenza, measles, rubella, mumps, whooping-cough, encephalitis lethargica and possibly chickenpox.

Group B Infectious diseases for which concurrent disinfection is required, terminal disinfection is unnecessary but special disinfection measures are required—Diphtheria, enteric and paratyphoid fevers, dysentery and poliomyelitis. The infective agent may persist on fomites rather longer in this group than in the previous one. Most authorities practice terminal disinfection, but all that should be necessary is a thorough soap and water cleansing.

Group C Diseases requiring concurrent and probably terminal disinfection—Scarlet fever.

Group D Diseases definitely requiring terminal as well as concurrent disinfection—Tuberculosis, anthrax and smallpox.

CONCURRENT DISINFECTION—In concurrent disinfection, the articles that require special attention are handkerchiefs, cutlery and crockery.

The following information is extracted from the Medical Research Council War Memorandum No. 11, on "The Control of Cross Infection in Hospitals", which is a mine of information likely to be useful to practitioners.

For general disinfection, the crude coal tar disinfectants of the "black fluid" and "white fluid" type should be used. More highly purified coal tar disinfectants, e.g., chloroxylenol (proprietary preparations, Dettol, Kilsol, O-syl, etc.) which are in short supply and expensive should be reserved for special purposes, such as disinfection of the hands. If of the same efficiency, as judged by the Chick-Martin coefficient, "black" and "white" fluids are equally suitable for most purposes. Black fluids cause staining and therefore white fluids must be used for linen and unstained wood. Examples of proprietary black fluids are—Antifect, Bactocene, Coetas, Disolite, Exenol superior, Hycol, Hygenol fluid disinfectant, Ialine special, Jeyes' fluid. Some of the proprietary white fluids are—Baxol X, Betazone No. 1, Evenol D.A. white, Ialine No. 8, Izal, Jeyes' white cylin.

For general purposes black or white fluids having a Chick-Martin coefficient of 30

diseases is one of the prices to be paid. One improvement which many practitioners would welcome is an extension to the county schools of the practice followed at some of the private schools, whereby the occurrence of a case in a class or department is notified to the parents of all the other children with the object of warning them not to send their children to school if suspicious symptoms appear. Often, however, a parent would, on his practitioner's advice, exclude from school a child in whose case, on account of some recent illness or impaired state of health, it was particularly important that all risk of infection should be avoided. The risk of infection in school could be reduced by improved ventilation of school buildings. Under the new School Building Regulations, the air in class-rooms has to be changed six times per hour, which will be a welcome improvement in the atmosphere too often found in the old schools with their high ecclesiastical windows, only a small part of which can open. The introduction of modern dust-reducing methods to schools should be taken up by the Ministry of Education, as there are good grounds for believing that further control of infection would result.

PREVENTION

In the more common infectious diseases of childhood, particularly measles and whooping-cough, it has been shown time and again that the case mortality falls as age increases, and therefore every effort should be made to secure that young children are safeguarded from exposure, so that the age of attack can be postponed.

Diphtheria —The case for active immunization at the age of twelve months has been established to the satisfaction of all reasonable people. The risk of a severe infection can be practically eliminated, whilst deaths from the disease among adequately immunized children are almost unknown. In this country it is usual to immunize children at about the anniversary of the first birthday. H. J. Parish, in a personal communication of January 1941, informed me as follows —

"It is usually stated that the optimum time for immunization of infants is towards the end of the first year of life, say, between the ninth and twelfth month. If you specially desire to immunize infants between the sixth and ninth month, there is little one can say by way of criticism because the majority of subjects will respond, although probably less well than they would three months later."

As there was a chance that some children would not respond so well as they would do three months later, I advised my staff to postpone immunization until about the anniversary of the first birthday. In America, the official recommendation is that immunization should be completed by the age of six months.

Alum precipitated toxoid is the prophylactic used by the Ministry of Health, who recommend a dose of 0.2 c.c.m., followed after an interval of about one month by 0.5 c.c.m. The injections are usually given intramuscularly into the left arm. A "boosting" dose of 0.5 c.c.m. should be given two or three months before entering school. Local authorities usually issue a certificate of immunization and advise parents to preserve it so that, should the child subsequently suffer from a sore throat, the medical attendant can see what prophylactic treatment has been carried out. In some counties arrangements have been made for the immunizing injections to be given by general practitioners in the rural areas where access to a clinic is not convenient. A great advance in the campaign would be gained if an effective one-shot method could be found, for the work would be much simplified and the acceptance rate improved.

Measles —As mentioned earlier, the aim should be to postpone the age of attack,

preferably until after the age of two years. Either attenuation or complete protection can be secured, but the latter should be reserved for children in whom even a mild attack might not be free from risk. Convalescent serum is preferable but not so easily obtained as pooled adult serum, which can be supplied by the local authority through the Emergency Public Health Laboratory Service. To obtain protection, treatment must be given within five to six days of exposure, which means within one or two days of the appearance of the rash in the original case. For protection, the dose of pooled adult serum for a child under three years is 10 c cm., and for attenuation, half this dose is given. After the age of three years, the dose is reckoned in c cm. by multiplying age in years by four. In practice, the first six days after exposure has often passed before the medical attendant has been consulted and consequently the choice is restricted to attenuation. In these circumstances, the same dose must be used as for protection, but prophylaxis after the ninth day is of no value. Attenuation and complete protection would be practised more frequently if the serum were more easily procurable and if smaller doses were needed. A remarkable advance has been gained by the development of Cohn's globulin fraction which contains natural antibody concentrated ten to thirty times and has given good results in America, both in protection and attenuation. It is hoped that this or a similar prophylactic will soon become widely available to general practitioners by local authorities in the same way as diphtheria antitoxin is at present available. Since, however, passive immunity is of temporary duration only, what is really wanted is a method of conferring active immunity.

Whooping-cough—Many practitioners are satisfied that protection, or at any rate attenuation, can be obtained by the use of vaccines. Cruickshank (1942) quotes the results of immunization against whooping-cough in the Faroe Islands epidemic of 1939: in this outbreak, the infection was mild or severe in 46 per cent. of the unvaccinated and in only 2 per cent. of the vaccinated. In America, the use of vaccines has become increasingly popular and in the Official Report (1945) of the American Public Health Association, their use is officially recommended for children in the early months of life.

In this country, the Whooping-Cough Sub-Committee of the Preventive Medicine Committee of the Medical Research Council has, since 1942, been carrying out trials. McFarlan, Topley and Fisher (1945), in a report on a series of trials in children attending infant welfare centres, day nurseries and in residential nurseries, found that the use of vaccines showed no significant difference in the incidence or severity of the disease between the inoculated and the controlled children. In these trials, a vaccine prepared in England was used and a fresh investigation, in which a vaccine of American origin is to be employed, will be undertaken. In this country, the official opinion is that the use of vaccines is still in the experimental stage.

References

- Cruickshank, R. (1942) "The Control of the Common Fevers," London, p. 150.
 McFarlan, A. M., Topley, E., and Fisher, M. (1945) *Brit. med. J.*, 2, 205.
 Murchison, C. (1862) "Treatise on the Continued Fevers of Great Britain," London.
 Savage, Sir William (1941) "Practical Public Health Problems," London.
 Wright, J., Cruickshank, R., and Gunn, W. (1944) *Brit. med. J.*, 1, 611.
 Extensive use has been made of the Medical Research Council's War No. 6 and No. 11, Sir William Savage's "Practical Public Health Problems," and "Control of the Common Fevers" published by the *Lancet* (1942).

group of normal children might produce a similar group of girls with raised sedimentation rates. The practical implication of the investigation is that too much reliance must not be placed upon one test; the patient as a whole must be carefully considered in coming to a decision as to whether the rheumatic infection has subsided sufficiently to allow of increased physical activity. Another recent observation that may have an important bearing on the significance of the sedimentation rate in rheumatic fever is that of F Homburger (*loc cit*, p 168) who has shown that *in vitro* sodium salicylate causes a marked reduction of the sedimentation rate.

PENICILLIN IN THE TREATMENT OF ACUTE OSTEOMYELITIS

SATISFACTORY results from the use of penicillin in the treatment of acute osteomyelitis are reported by W A Altemeier and J A Helmsworth (*Surgery, Gynecology and Obstetrics*, August 1945, 81, 138). Their observations were made on thirty-four patients, thirty of whom were under the age of thirty. In twenty-five instances the long bones were involved, whilst three had involvement of the pelvic bones, five had involvement of the facial and cranial bones and in one case the ribs were infected. The infecting organism was determined in thirty-three cases: haemolytic *Staph aureus* was isolated in twenty-nine cases, non-haemolytic *Str albus* in two, *Str haemolyticus* in one, and pneumococcus type III in one. Positive blood cultures were obtained in twenty cases. Penicillin was given by continuous intravenous drip (ten cases) or by interval intravenous or intramuscular injection, the recommended total dosage being 1,500,000 units or more administered over a period of two weeks or longer. There was only one death in the series: a severe and neglected case with staphylococcal bacteraemia and pneumonia admitted to hospital fourteen days after the onset of the illness, death occurred seventeen hours later. From the point of view of therapy, cases of acute osteomyelitis are divided into four groups. *Group I*—cases diagnosed early and adequately treated with penicillin respond well to treatment with a minimal amount of residual bony damage, surgical intervention is not required. *Group II*—moderate delay in diagnosis increases the amount of bony damage, but results with penicillin are satisfactory without surgical drainage. *Group III*—when delay in treatment exceeds seven to ten days, sequestration usually occurs and large abscesses may form and require surgical drainage. *Group IV*—certain fulminating cases unlikely to survive sufficiently long for penicillin therapy to be effective. These require surgical intervention as an emergency measure, in addition to full doses of penicillin. A point

stressed by these observers is that bony change continue after the cessation of penicillin treatment, so that a month after such therapy has been discontinued the radiological appearance of the bone appears worse than when penicillin was being given. They suggest that this is due to penicillin converting an area of septic necrosis into one of aseptic necrosis.

NEW DRUGS FOR TRIAL IN LEPROSY

AMONG the drugs discussed under this heading in the *Leprosy Review*, August 1945, 16, 4, are diason and penicillin. The former is a synthetic preparation in the form of a white powder which may be given by mouth or, dissolved in normal saline and filtered, by intravenous injection. With the use of this drug two dangers must be guarded against, i.e., the production of haemolysis and secondary anaemia, and inflammatory reaction in the lesions. For this reason frequent blood tests are necessary, preferably the red cell count but, failing this, the haemoglobin estimation may be relied upon. If no intolerance is shown, diason should be given on alternate days, thrice weekly. The usual initial dose employed in the report quoted was 0.6 gm., rising to 2.6 gm. when given intravenously. 1 gm. was dissolved in 3 c.cm. sterile normal saline and the solution filtered. In patients with a haemoglobin of less than 70 per cent. the maximum dose was 1.3 gm., and ferrous sulphate, 4 grains twice daily, was given. Patients who showed progressive anaemia were given injections of liver extract and the diason was either stopped temporarily or the dosage reduced. The importance of keeping patients undergoing treatment with diason under observation is stressed. The best results obtained with the drug were in advanced lepromatous cases, in many of which the ulcerating lesions healed rapidly, the temperature became normal and the general condition improved. Penicillin has been used by L H Wharton, Medical Superintendent of the Mahana Leprosy Hospital, British Guiana, in two series of cases. In the first series, 100,000 units were given over a period of 60 hours and produced marked improvement in the complications of leprosy and in the blood sedimentation tests. The second series, consisting of nine patients with advanced leprosy, was treated with higher dosage: three patients were given 400,000 units each of sodium salt of penicillin, in the form of intramuscular injections of 10,000 units three-hourly, and six patients were given 200,000 units each, by intramuscular injection of 5,000 units three-hourly. There was a marked increase in the appetite and a feeling of drowsiness during the treatment. No rise in temperature occurred and there was no complaint of undue pain at the site of injection. In conclusion, it is stated that although

penicillin in total dosage of 400,000 units is not bactericidal or bacteriostatic to *Bacillus lepra*, the drug is of definite value in the complications of leprosy, and the marked improvement obtained in the physical and mental conditions of the patients with advanced leprosy would justify its use

THE TREATMENT OF HERPES ZOSTER BY SYMPATHETIC BLOCK

According to T Findley and R. Patzer (*Journal of American Medical Association*, August 25, 1945, 128, 1217) blocking the appropriate sympathetic ganglia with procaine hydrochloride is one of the most effective means of abolishing the pain of herpes zoster. They report four cases, three adults and one child, in whom relief from pain was instantaneous and permanent, in two of the cases the herpes occurred in the lower cervical or upper thoracic segments, whilst in the other two it was in the lower thoracic or upper lumbar segments. A full description is given of the technique for infiltrating the cervico-dorsal and second and third thoracic sympathetic ganglia by the anterior approach, this procedure is said to be relatively easy to carry out and to be without danger if only procaine or allied anæsthetic drugs are used. It is suggested that such regional sympathetic block relieves the pain of herpes zoster by abolishing segmental vasospasm.

A SIMPLE TEST FOR ACETONURIA
A SIMPLIFICATION of the well-known Rothera's test for acetone in the urine is described by I. M. Rabinovitch (*Canadian Medical Association Journal*, June 1945, 52, 602). The reagents are incorporated in a well-compressed tablet (3/8 of an inch in diameter) in the following proportions—

Sodium nitro-prusside	15 parts
Sodium carbonate (anhydrous)	285 "
Ammonium sulphate	450 "
Binder (lactose)	250 "

When this tablet is added to a test tube containing urine with acetone, a definite permanent blue discoloration develops on the under surface of the tablet within one to three minutes, the intensity depending upon the amount of acetone bodies present; the upper surface of the tablet remains white. Having used this method in more than 1,000 examinations of urine, the author is convinced of its reliability and sensitiveness. The tablet is stable and keeps well. A further simplification of the test is also described which dispenses with the need for test tubes. The tablets are made with a depression in one side, and one drop of urine is placed in this depression. If the urine contains acetone bodies, the centre of the tablet becomes per-

manganate in colour in one to three minutes, the rest of the tablet remaining white.

THE PROGNOSTIC SIGNIFICANCE OF THE ELECTRO-ENCEPHALOGRAM IN WAR NEUROSIS

THE increasing use in America of the electro-encephalogram (E.E.G.) as a routine method of investigating the neuroses led M. E. Heppenstein, D. Hill and E. Slater (*Brain*, 1945, 68, 17) to investigate the E.E.G. in 300 soldiers who were passing through a neurosis rehabilitation centre. These men were followed for at least fifteen months, and an attempt was made to correlate the E.E.G. and the patient's subsequent progress. Ten of the records were discarded for technical reasons. Of the remaining 290 cases, 59 were subsequently invalidated, 58 were last heard of on light duty and 173 were on full duty. Of the E.E.G.'s, 121 were normal, 70 were doubtful and 99 showed a non-specific abnormality. There was, however, no evidence that normality or abnormality of the E.E.G. was associated with a satisfactory or unsatisfactory follow-up record. It is therefore concluded that the use of the E.E.G. in screening Army entrants, or soldiers who have suffered a neurotic breakdown, can only be engaged in "with the utmost caution."

THE DANGERS OF BORACIC ACID

THE report of a fatal case of boracic acid poisoning, following the use of boracic acid ointment in eczema, by C. H. Watson (*Journal of the American Medical Association*, September 29, 1945, 129, 332), again draws attention to the dangers of this drug. There have been many reports in the medical literature of boracic acid poisoning, either accidental or following its use in ointment, powder or solution form. After two incidents of poisoning among infants in hospitals (one involving nineteen infants, with four deaths, and the other two cases, both fatal) the Director of Public Health of Illinois requested hospitals to remove boracic acid from the list of drugs kept for use in maternity hospitals. Boracic acid solution is commonly used for irrigation of the eyes and body cavities, and it is not perhaps generally recognized that a weak solution of sodium bicarbonate is more effective for removal of pus from the eye. Mothers commonly use boracic acid solution for bathing their babies' eyes freshly boiled and cooled water is equally effective. Another use of boracic acid solution is for cleansing the breasts before feeding; this involves danger from reliance on the supposed bactericidal action of the drug. In the words of the author, "use of boric acid preparations should be discouraged because of their limited usefulness and the risk of both accidental and intentional use."

REVIEWS OF BOOKS

A History of Medicine By DOUGLAS GUTHRIE, M D, F R C S E D, F R S E Edinburgh Thomas Nelson and Sons Ltd, 1945 Pp xvi and 448 Plates 72 Price 30s

THERE has of recent years been an increasing interest in the history of medicine, particularly among the younger generation. For those who, knowing little about the subject, wish to have a reliable guide, Dr Guthrie's new work can be thoroughly recommended. Using the biographical method, he traces the history of medicine from prehistoric times down to the turn of the 19th century. Although the biographical method is used, the book is not a mere collection of biographies, the steady development of medicine throughout the ages is unfolded era by era, taking the life of the outstanding representatives of each era to illustrate the predominant features. By this method a sense of perspective is maintained, yet the narration is never overcrowded with dates or mere lists of events. For the novice this is the ideal method, as it holds the reader's interest and allows him to appreciate the main trends without becoming lost in detail. Dr Guthrie has a pleasant style without ever becoming journalistic, although there is a tendency at times to the excessive use of the superlative. The book is well documented and the addition as an appendix of a classified bibliography of medical history provides a most useful guide for the reader who wishes to pursue his studies into special aspects of the subject. The standard of production is commendably high, and special praise must be given to the illustrations, which have not only been selected with much care and discrimination, but are also reproduced in a most attractive style. As an introduction to the history of medicine this work will take a high place in the annals of the history of medicine.

Duodenal and Jejunal Peptic Ulcer By RUDOLF NISSEN, M D London William Heinemann (Medical Books) Ltd, 1945 Pp 143 Figures 123 Price 21s

DR NISSEN's book gives the lessons of a long experience in gastric surgery. It is clearly and logically written, well and profusely illustrated, and well produced. The author writes as an American, but his training and outlook are of the German school, one that differs from the British in no branch of surgery more than this. He

assumes that all duodenal ulcers should be resected, whereas the generally accepted view is that all duodenal ulcers heal immediately when the flow is diverted from their site, and remain healed permanently. He states that as a surgeon's skill develops, the number of duodenal ulcers he considers non-resectable decreases, conversely here it is usually found that as a surgeon's skill develops the number of duodenal ulcers he wishes to resect sinks to vanishing point. He advises removal of only half the stomach because a high resection has a high mortality; here it is considered that the dangers of gastrectomy for duodenal ulcer are connected with the duodenum and not at all with the level of gastric section, whereas the post-operative failures are all among the conservative gastrectomies. He rejects gastro-jejunostomy as having a mortality of 7 per cent and a recurrence rate of 12 to 20 per cent; experience in this country tends to show that jejunal ulceration follows only those short circuits wrongly done for acute ulcers in young people, and that when performed for proper indications, gastro-jejunostomy is a trouble-free operation, safer and more satisfactory than gastrectomy. Yet even those who disagree with the author's main premises cannot fail to find interest in this book, and learn many valuable expedients from its pages. Such important questions as the method of dealing with ulcers that are bleeding actively at the time of operation, the way to close a duodenum after a posterior ulcer has been laid open, or to overcome the disaster of a duodenum divided too short for infolding, the many problems that arise in handling jejunal ulcerations and gastro-jejuno-colic fistulae—all these are dealt with in practical fashion and in full detail. It is a book for the surgeon's personal library.

Anatomy as a Basis for Medical and Dental Practice By DONALD MAINLAND, M B D Sc London Hamish Hamilton Medical Books, 1945 Pp xvii and 863 Figures 61 Price 35s

PROFESSOR MAINLAND of Dalhousie University Halifax, has, deservedly, the reputation of a sound and successful teacher, and the publication of this book makes available to a wide constituency those notes which he has used to guide and inspire successive groups of his own students. The long list of well-chosen references provides reassuring evidence that there still exists a generation of British anatomists who, like the

author, in their enthusiasm for teaching the right kind of anatomy to medical and dental students, have not sacrificed their scientific and practical outlook. This book is packed full of sound advice and useful information, and though its use will involve "hard work and hard thinking—because it contains ideas and problems as well as facts", in this quality is the justification for its publication. The reader will not find his study of anatomy made any easier but he will find his toil rewarded with just that useful and practical knowledge of human anatomy which his clinical studies in future life-work require. A series of questions drawn up in connexion with each section of the book challenge the reader, not as perfunctory examination formula, but as a test of his powers of reasoning and reflection, and are well calculated to reveal to him the implications of the facts which his reading has just presented to him. This plan is admirable. It is disappointing to find a book like this so meagrely illustrated but it is clearly meant to be used in combination with a good atlas and, better still, in constant association with the work of the dissecting-room. As a protest, where such is necessary, against the idea that the study of anatomy is just the memorization of factual knowledge without reference to its vital relation to the whole fabric of medicine, this book merits commendation.

NEW EDITIONS

THE second edition of *Handbook of Diagnosis and Treatment of Venereal Diseases*, by A. E. W. McLACHLAN, M.B., CH.B., D.P.H., F.R.S. (E & S Livingstone Ltd., 15s) contains, among other additions, new information concerning the interpretation of serological tests for the diagnosis of syphilis. Although the first edition appeared in 1944, the use of penicillin, in the treatment of both syphilis and gonorrhoea, has made great strides in the interval. These advances have been incorporated in the chapters dealing with the different forms of venereal disease. Considering the importance of this new weapon in the fight against venereal disease, it is perhaps a pity that a separate chapter has not been devoted to the subject, but no doubt this will be rectified when the end-results are more clearly indicated. The illustrations, some in colour, which number 159, are well produced.

Eleven years have elapsed since the appearance of the first edition of *The Rheumatic Diseases*, by G. D. KENSLEY, M.D., F.R.C.P., much revision has been undertaken in the preparation of the second edition (William Heinemann

(Medical Books) Ltd, 15s). A fresh system of classification, based on clinical syndromes and etiology, has been adopted. New chapters dealing with the interrelationship and etiology of rheumatic diseases, the types of specific infective arthritis, and conditions simulating arthritis, have been added, and in the chapter on special treatment there is a particularly interesting section devoted to hydrotherapy.

AMONG new additions to the eighth edition of *Medical Jurisprudence and Toxicology*, by JOHN GLAISTER, J.P., D.Sc., M.D., F.R.S.E.D. (E & S Livingstone, Ltd, 30s) are sections on the presumption of survivorship, in which the Grosvenor case is cited as example, the proposed social insurance system, new information, from the forensic point of view, concerning the M, N and Rh blood factors, and the incorporation of new poisonous substances in the section devoted to toxicology. In spite of a somewhat stormy production period, the new edition emerges triumphant. The addition of a number of new illustrations is an added attraction.

THE third edition of *Kettle's Pathology of Tumours*, by W. G. BARNARD, F.R.C.P., and A. H. T. ROBB-SMITH, M.D. (H. K. Lewis & Co Ltd., 21s) is fittingly dedicated to the memory of the original author. The lapse of twenty years since the appearance of the second edition has necessitated much revision and the inclusion of advances in the experimental and histological study of tumours. The work is too well known as a textbook to call for detailed description, but mention may be made of much interesting information on the incidence of cancer included in the chapter devoted to etiology. In spite of the many advances in the diagnosis and treatment of cancer there is no evidence of decreased incidence among males during the period 1911-40, and there has been a marked increase in the incidence of cancer of the lung during that period, the Registrar-General's figure for deaths among males from this cause being 12.7 per million for the period 1911-20, followed by a steady increase up to the figure of 109.2 per million for the period 1936-40. The figures for deaths from cancer among women during the period 1911-40 show a slight decrease in the total, but here again there is a steady increase in the number of deaths from pulmonary carcinoma, although on a much lower scale—7.0 per million for the 1911-20 period gradually rising to 25.7 per million for the years 1936-40. The new edition, which will be assured of a warm welcome, is richly illustrated, containing in all 191 figures.

NOTES AND PREPARATIONS

NEW PREPARATIONS

'MICKRAFORM' SULPHATHIAZOLE SUSPENSION is a sterile 20 per cent suspension of micro-crystalline sulphathiazole in isotonic saline, stable, non-alkaline and non-irritating. The advantages claimed for the administration of sulphathiazole in the form of the mickraform suspension are enhanced therapeutic effect, ability to permeate deep wounds and body cavities, and the chemical stability and correct pH of the suspension. It is issued, on prescription only, in 25 c.c. bottles containing 5 gm sulphathiazole, preserved with 0.001 per cent phenylmercuric acetate, by Menley & James Ltd, 119-123 Coldharbour Lane, London, S.E. 5, from whom literature can be obtained.

NEW APPARATUS

BONOCORD HEARING AID MODEL P 4, is a vest-pocket amplifier which, on account of its improved circuit design, new wide-range, shock-proof crystal microphone, greater sensitivity and



improved high frequency response, is stated to represent a considerable step forward in modern hearing aid technique. With a maximum output of 75 decibels, a three-stage amplification, independent switch and volume control, and a background noise suppression circuit, model P 4, the size of which is $4\frac{1}{2}$ by $2\frac{1}{2}$ by

$\frac{7}{8}$ inches, is claimed to be light and pleasing to both eye and ear. The price of the new model is 22 guineas. Further particulars and literature can be obtained from the manufacturers, Allen & Hanburys Ltd, 48 Wigmore Street, London, W. 1.

A NEW ANTI-MALARIAL DRUG

PALUDRINE, until recently known as 4888, belongs to a group of compounds previously unexplored for anti-malarial activity, and is not a quinine substitute. Its discovery is the result of research work carried out by a team of chemists and biologists from the laboratories of Imperial Chemical Industries Ltd. In collaboration with the Medical Research Council the drug has been subjected to clinical trial at the Liverpool School of Tropical Medicine, one hundred cases having been treated since January 1945. Later the drug was flown to

Australia for more extensive trials, the results of which confirmed those reported from Liverpool. Paludrine is stated to be more effective than quinine or mepacrine and of low toxicity; it is easy to manufacture and, being colourless, does not produce the yellow effect noted in patients treated with mepacrine. The results of more prolonged trial to determine the new drug's efficacy in the prevention of relapse will be awaited with interest.

OFFICIAL NOTICES

Rickets. The Ministry of Health has issued a memorandum on this subject, prepared by the British Paediatric Association and dealing with the etiology, diagnosis, prophylaxis and treatment of rickets. *Staff for Tuberculosis Institutions* (Circular 166/45) and *Tuberculosis—Service Cases* (Circular 177/45) deal, in the first instance, with the examination and tuberculin testing of nurses and domestic staff engaged in tuberculosis institutions, and in the second with the question of liability for the cost of sanatorium treatment for members of the Forces.

BACK NUMBERS OF THE PRACTITIONER FOR DISTRIBUTION IN DEVASTATED COUNTRIES

SEVERAL appeals for medical literature have been received recently from members of the medical profession who during the war years have been almost entirely shut off from current medical events. The following letter from Hong Kong is a typical example—

"As a prisoner of war I was cut off from all medical reading for three years and eight months. It will take a long time to catch up, especially when one is tired out in brain and body! I wonder if any of your readers have some back numbers they could spare one who is hungry for fresh light? If so, I would be more grateful than I can say."

Any back numbers which subscribers or readers no longer need will be gratefully received at 5 Bentinck Street, London, W. 1, for such cases, and for distribution through official sources in devastated countries, particularly in Holland, Czechoslovakia and Poland, where at the present time medical literature is practically non-existent. The receipt of copies will be acknowledged and, when possible, indication of the proposed recipients given.

INDEX TO VOLUME 155

COPIES of the index and title page to volume 15 (July-December, 1945) are available on application.

CONTENTS FOR JANUARY 1946

In future, the contents for the succeeding issue will appear on the last page of the advertisement section, in this instance on page LXVI.

